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SIGNIFICANCE OF SYSTOLIC CARDIAC MURMURS IN COLLEGE STUDENTS*

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AS ONE becomes interested in heart disease, the many problems connected with the cardiac status among young people demand attention. Questions frequently arise concerning young persons that do not occur so often in older age groups. Many times one is faced by the question of how to interpret a heart murmur. Does it or does it not mean organic heart disease? If it does, what type of restrictions are demanded and what sort of life should this person lead?

If one is to avoid injustice and serious injury to the future of these young people, he must carefully weigh all the evidence before making a diagnosis of organic heart disease. With the increasing interest in matters pertaining to health, such as high-school and college physical examinations, industrial-health requirements and more particularly Selective Service examinations, more and more problems concerning the interpretation of cardiac findings are sure to arise. A national attitude toward these findings must be assumed. Certainly it is a greater error to make the diagnosis of an organic heart lesion in a person with a normal heart than it is to make one of a normal heart in a person with a minimal valve lesion without any other cardiac finding. In the first case, not only is the way paved for the making of a cardiac neurotic but also the course of an otherwise normal life may be changed to one that becomes a burden to the patient and to society. On the other hand, the amount of damage done to a heart with minimal valve lesions and no evidence of active rheumatic fever is probably nil under ordinary physical strain.

The physical sign that causes the most difficulty in evaluating the cardiac status of a young person is the systolic murmur. The exact mechanism involved in the production of such murmurs is not understood. It may be assumed that a good many of them are due to stenosis of the various heart valves, namely, aortic, pulmonary or tricuspid stenosis. Likewise, congenital defects may be responsible. In many cases the murmur may be due to hypertension or to arteriosclerosis, dilatation, or atheroma of the aorta, without valvular lesions. One not infrequently hears a very loud systolic murmur all over the precordium, in some cases with a pronounced thrill, and discovers perfectly normal heart valves at autopsy, so that no satisfactory explanation of the murmur is found. If this is true of pronounced systolic murmurs, a murmur of much less intensity must be interpreted with even greater caution as meaning organic heart disease. Most examiners interpret as functional all systolic murmurs over the pulmonic area of Grade 2 or less.[1] In addition, many physicians disregard soft systolic murmurs over other parts of the precordium, provided no other signs or symptoms of heart disease are present. However, in routine examinations one frequently hears a systolic murmur that because of its intensity, location and so forth causes concern. In this study an attempt was made to evaluate systolic murmurs in young people.

MATERIAL AND METHOD OF STUDY

The Department of Hygiene at Harvard University has afforded the opportunity to make a study of the cardiac status of youths in their late teens who represent a good cross section of native Americans, both socially and geographically, although probably on a higher economic level than the average youth. Through this department, each Harvard freshman is required to have a routine physical examination by specially qualified physicians. Before the student appears for examination, as much information as possible about his previous health is obtained from the parents. A detailed history is then elicited by the examiner.

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The following points in the cardiac examination are stressed: a possible history of rheumatic fever or any known form of heart disease; any past restrictions in physical activities because of "heart trouble"; the size of the heart and the rate, rhythm and blood pressure; the presence or absence of murmurs and, if present, the area where best heard and the kind and intensity of the murmur.

The first group selected for this study was the Class of 1941, numbering 946 students; the second group was the Class of 1942, numbering 938 students; and the third group was the Class of 1943, numbering 972 students. This made a total of 2856 students examined.

Results

Incidence of Rheumatic Fever

Of these 2856 subjects, a definite history of rheumatic fever was obtained in only 13 cases, or less than 0.5 per cent of the total group. In addition, 1 student developed rheumatic fever for the first time while attending college. This low incidence of previous rheumatic fever is noteworthy, especially since a fair number of the students were born and reared in the region of the northern Atlantic seaboard.

Careful examination of the group with a previous history of rheumatic fever showed no cardiac murmur whatsoever in 5. Five subjects had systolic murmurs that were barely audible and confined solely to the pulmonic area; 2 had definite evidence of valvular heart disease, and 1 was classified as having possible mitral stenosis.

Spurious Heart Disease

The most interesting and important group consisted of 26 students who, previous to entering college, had been restricted in physical activity because of so-called "heart disease." The majority of the cases were brought to attention by letters from the family before the students appeared for routine examination. These letters usually contained statements that the youth in question had a "bad heart" and must be careful not to overexert himself. In most cases, so far as could be learned, the diagnosis of "heart trouble" had been made years before by the family doctor, usually because of the presence of a systolic murmur. Among these 26 students in 7 no murmur whatsoever was heard, nor were there any other abnormal cardiac physical signs. Three of the 7 had a previous history of rheumatic fever. Fourteen students had only a very soft systolic murmur at the base or apex, without any other evidence of heart disease. One had benign extrasystoles. Two had evidence of active rheumatic heart disease with valvular lesions, and 2 had the physical findings of congenital heart disease. Thus, only 4 of the 26, or 15 per cent, had organic heart disease. On the other hand, 22 (85 per cent), on the most careful examination, including 7-foot heart films and electrocardiograms in the doubtful cases, were found to have no heart disease. Thus it seems that a great many young persons are classified as having organic heart disease when it does not exist. Moreover, these young men are unnecessarily restricted from the usual activities of their age. This is certainly not conducive to good physical and mental health, and in some cases the personality is definitely warped. On the other hand, it should be remembered that youths who have had rheumatic fever and previous evidence of acute or subacute myocarditis may give no indication of organic heart disease at some subsequent examination.

Systolic Murmurs

In the entire group of 2856 students, a systolic murmur of some degree was heard in 350 cases (12.3 per cent). In 208 (7.3 per cent of the total), the murmurs were of such character and intensity that they were classified as functional by the examiner, and the subjects were therefore dismissed as having normal hearts. In 9 cases (0.3 per cent of the total) the cardiac findings led to a positive diagnosis of inactive rheumatic heart disease with valvular lesions. Six (0.2 per cent) had congenital lesions. The remaining 127 subjects (4.6 per cent of the total) had systolic murmurs of such intensity and location that they were not classified as functional, nor were the findings sufficient to make possible a diagnosis of organic heart disease.

It is in the last type of person that careful study, history-taking and intelligent interpretation of the findings are necessary if one is to avoid error. In order that as much information as possible might be obtained for this purpose, all these students were subsequently seen and examined by me and followed at regular intervals. The cardiac examination consisted of heart size, rhythm, rate, blood pressure, character and intensity of murmur and the area in which it was best heard. The examination was made with the patient lying on his back, on his left side, sitting and after exercise. The intensity of the murmur and the area in which it was best heard were recorded according to the method of Freeman and Levine.[1] In all cases where there was doubt as to cardiac size, a 7-foot heart film was taken. Likewise, if there was any disturbance of rhythm, an electrocardiogram was taken. In no case was any abnormality found in either the heart film or the electrocardiogram. The majority of these students were fol-

lowed at six-month intervals, with a cardiac examination at the end of each period. Thus, it was possible to follow the group from the Class of 1941 for four years, that from the Class of 1942 for three years, and that from the Class of 1943 for two years.

In analyzing these cases, it was found that the systolic murmur was most pronounced at the pulmonic area in 50 per cent of the cases and at the apex in 39 per cent, and was of equal intensity in both places in 11 per cent. The murmur was invariably intensified after exercise, with an increase in heart rate. Likewise, in most cases the murmur was more pronounced in the supine than in the sitting position. However, the position, the area in which the murmur was best heard and its relation to exercise were not enlightening concerning whether the murmur was organic.

These students were allowed unrestricted activities, and during the follow-up study no noticeable change in cardiac findings occurred. Moreover, in no case was a diagnosis of valvular heart disease subsequently made.

Systolic Murmurs and Exercise

As stated previously, none of the students with systolic murmurs alone were restricted in exercise. However, one is frequently forced to make decisions concerning how much and what kind of exercise and so forth are to be permitted when a student has an unusual cardiac finding. This is illustrated in the following two cases.

G. H., aged 19, had rheumatic fever three times in childhood, the last attack at the age of 13. He was thoroughly studied at the Presbyterian Hospital, New York City, in 1932, at which time all the studies were normal with the exception of a moderately rough, Grade 2 systolic murmur over the precordium, best heard at the apex. No diastolic murmur was heard. In 1937, when he reported as a freshman, the same cardiac findings were present. There had been no intervening history of rheumatic fever. Fluoroscopic examination of the heart was normal in all respects. The white-cell count and sedimentation rate were normal, and so far as we were able to ascertain, there was no difference in the heart findings in 1937 and those of the previous 5 years. The student was eager to be allowed to play football. This was permitted, with the understanding that he would report at least twice a year for a cardiac check-up. During his 4 years in college he played freshman and varsity football. At no time was there any change in the cardiac findings, nor were there any evidences of smoldering rheumatic infection.

L. M., aged 18, had a negative past history, with no evidence of rheumatic fever or chorea. He had always been active in sports, and played football and basketball in high school. During his routine physical examination the heart seemed clinically enlarged, the rate was slow (68), and the blood pressure was 110/70. There was a marked sinus arrhythmia, and a rough, Grade 2+ systolic murmur was audible over the precordium, best heard over the pulmonic area. No diastolic murmur was heard. Fluoroscopy and a 7-foot heart film showed no enlargement and no abnormality in contour. Electrocardiograms were also normal. This student was eager to play football. He was allowed to do so, but his cardiac status was closely followed. A recent complete cardiac examination, including fluoroscopy and x-ray, showed no change since the original examination 3 years before.

It is my opinion that playing football has not injured either of these students, nor has it caused any progression in their cardiac ailments.

Summary

The cardiac status of 2856 Harvard College students was evaluated as accurately as possible by a careful history and physical examination. When indicated, fluoroscopy, electrocardiograms and follow-up studies were done.

Three hundred and fifty (12.3 per cent) of the total group were found to have a systolic murmur. In 208 (7 per cent) the murmur was classified as functional at the time of the original examination and the cases were not studied further. In only 9 cases was it possible to make a diagnosis of inactive rheumatic heart disease with valvular lesions. In 6 cases a diagnosis of congenital heart disease was made.

One hundred and twenty-seven students (4 per cent) had systolic murmurs of such intensity or character that the original examiner was unwilling to diagnose them as functional. A good many of these subjects were carefully studied and followed for two to four years, and in no case was it possible to make a diagnosis of organic heart disease, although such, of course, may have been present.

A fairly large number of boys were studied who had previously been restricted in their activities because of heart disease that did not exist.

In 2 cases the relation between exercise and "heart murmurs" is discussed in some detail.

Conclusions

The incidence of previous rheumatic fever and inactive rheumatic heart disease among Harvard College students is very low.

Apparently, the diagnosis of organic heart disease is made too frequently when it does not exist.

Likewise, the restrictions placed on persons with minor valve deformities is probably too rigid, and may inhibit an otherwise normal program, both physical and mental.

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DEATH FROM ALLERGIC SHOCK*

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IT IS the purpose of this paper to consider a recent case of a fatality following the intradermal administration of a minute amount of foreign-proteid material, investigation of which revealed a hereditary relation to an earlier case, the history of which is drawn from the literature. As other factors in the case histories must be interpreted against the patients' common heritage, it is thought that together they may contribute evidence of value to students of atopic allergy.

Moreover, such accidents, though rare, are now largely avoidable if the parenteral administration of foreign-proteid matter is preceded by adequate history-taking, careful tests and thorough physical examination, and if, when attempted, it is discreetly done with appropriate remedies at hand to combat reactions. Not one but all these precautions constitute the "due care" imposed on the practitioner legally as well as ethically.

In Massachusetts, such fatalities come under the jurisdiction of the medical examiner. It was such an investigation in line of duty that developed the facts that this paper sets forth. In a previous communication[1] use has been made of special features of the investigation of interest to pathologists and immunologists. In this one an attempt is made to develop such features as may bear on the work and responsibilities of the clinician.

On August 27, 1940, the medical examiner of Worcester County received a call from a hospital for the insane, where an accident had occurred incident to a carefully planned research designed to determine the rate of cutaneous color-spread among schizophrenics as compared with normal persons. A physician had assembled a group of young women from among the employees. The nature of the investigation was explained to them and a fee was allotted to each. No danger was anticipated, but all the subjects were questioned concerning allergic sensitiveness and previous immunizations, to which negative replies were made in all cases. Physical examinations and eye and scratch tests had not been made, since they were not thought necessary. The test solution was guinea-pig hemoglobin, selected because of its known low antigenic power. The hemoglobin was dissolved in physiologic saline solution and made up to a volume equivalent to that of the quantity of blood from which the corpuscles were originally derived. Only 0.2 cc. was given intradermally, a dose no greater than is often used clinically for sensitivity tests.

As the seventh subject was being injected, the fifth subject, A. D., a well-developed woman of 22, experienced respiratory distress and became cyanotic. The physician gave adrenalin and proceeded with his injections. The woman's condition soon became alarming. Adrenalin was injected into the heart and artificial respiration was applied, but to no avail, and the subject expired 10 minutes after receiving the injection.

The following is abstracted from the official report of the medicolegal investigation:

> I viewed the body as it lay clothed on the bed in the room where the testing had been done. None of the other young women who had received the test were feeling any ill effects. I examined the arm of one of them and saw a puncture mark surrounded by a brownish zone about 0.6 cm. in diameter, which in turn was surrounded by a narrow zone of edema. This was similar to though less intense than that on the dead woman's arm.
>
> In view of the seriousness and exceptional circumstances of the case, I felt that the official participants and witnesses to an autopsy prescribed by statute should be competent persons not connected with the institution. I therefore invited Dr. Alan R. Moritz, professor of legal medicine at Harvard Medical School, to co-operate with me in the autopsy. He and his associate, Dr. Herbert Lund, arrived at 5:00 p.m. The hospital facilities were placed at our disposal by the acting superintendent, Dr. William E. Barton.
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> The autopsy was begun about 5:30 p.m., Drs. Hunt, Moritz, Lund and Freeman participating.

The details of the post-mortem examination appear in the previous publication.[1] In summary, it revealed acute hemorrhagic inflammatory reaction at the site of a needle-puncture wound in the skin of the right forearm; edema of the mucosa of the air passages; mild laryngitis, tracheitis, bronchitis and pneumonitis; marked emphysema of both lungs, with the formation of large air-filled subpleural bullae; rheumatic carditis with mitral, aortic and tricuspid valvulitis (old); moderate arterial hypoplasia; and noninvolution of the thymus gland.

Despite the fact that sensitivity to guinea-pig protein is not common and that the dose given was extremely small, it was thought that the most tenable explanation of the fatal collapse was al-

*Read, in part, at the annual meeting of the Massachusetts Medico-Legal Society, Boston, May 26, 1942.

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lergic shock. Although it seemed possible that inflammation of the respiratory passages and chronic rheumatic heart disease may have contributed to the death, they did not in themselves provide an adequate explanation. It seemed highly desirable to demonstrate whether or not there was present in the blood a specific reagin to guinea-pig hemoglobin. To determine this point, it was decided to employ the method of local passive sensitization.

FIGURE 1. *Prausnitz–Küstner Reaction.*
The positive reaction is on the left, and the negative control on the right.

Accordingly, 20 cc. of blood was drawn aseptically from the right auricle, and with it Prausnitz-Küstner tests were carried out on 3 subjects by Dr. Lund in Dr. Moritz's laboratory.* A detailed report of the tests appears in the paper by Lund and Hunt referred to above. They were positive in 2 subjects, but the third proved nonreactive. Figure 1 shows the intensity of the reaction in comparison with the control as both appeared on the first subject (Lund). All the controls were negative. At a later date the sensitized area was tested to mixed duck, chicken and goose feathers, with negative results. The reaction to horse dander was also negative, but dog hair gave a positive reaction. This was confirmed some weeks later when an accidental scratch by a dog on the sensitized area was followed by a large wheal. The conclusion that A. D.'s blood contained reagins specific to guinea-pig hemoglobin and to dog hair therefore seemed to be justified.

As a result of the history, post-mortem examination and passive-transfer test, the cause and manner of death were officially returned as follows: "Anaphylactic shock following an intradermal injection of guinea-pig hemoglobin. An accident of medical research. . . . Investigation failed to discover evidence of any illegal act and further judicial inquiry is unnecessary."

Although this report concluded the official investigation, other aspects of the case were intriguing. From the woman's mother, hospital records and physicians under whose care A. D. had been, the following information was obtained. She had suffered from asthma for eight years and had shown positive cutaneous reactions to dog hair, kapok, shellfish, ragweed, timothy, orris root and house dust. Negative results were obtained with egg, milk, rabbit hair and chicken feathers. To her mother's knowledge the woman had never had any contact with guinea pigs. She had had symptoms in childhood that suggested rheumatic fever or infantile paralysis to the attending physicians. She had some physical signs interpreted as mitral stenosis, but there was no history of cardiac decompensation. She was a liberal but not excessive salt-eater, which would seem to rule out adrenal insufficiency.

The family history is extremely important. The mother had asthmatic attacks and symptoms of hay fever during one summer. A brother was subject to hay fever and a sister to acne. Two other sisters were normal. The brother was the only male of either the mother's or the father's line known to have been allergic. *A first cousin of the mother died in convulsions at the age of sixteen, ten minutes after a subcutaneous injection of diphtheria antitoxin.*

This patient, B. V., was also asthmatic. Her accidental death in Brooklyn, New York, in 1895

*I am indebted to these men, and accord them full credit for this ingenious application of a biologic test to the technic of post-mortem investigation.

was the first in this country to result from an injection of diphtheria antitoxin.

The story is graphically told by her physician, Dr. James L. Kortright,[2] as follows:

> On March 27, 1895, I was called to a little boy . . . almost moribund with malignant diphtheria. The family had not suspected the serious nature of his illness and had tried home remedies for five days before seeking professional help. He died the same day. When I announced the diagnosis, his cousin, a stout, well-nourished girl of sixteen [seventeen] years, asked me to examine her throat. There were a few spots occupying the crypts of the right tonsil. . . . On March 28 the temperature was 101°F. Nausea was present and there was a grayish exudate over both tonsils, extending upward to the pillars of the fauces and backward upon the pharyngeal wall. Bacteriological examination showed almost a pure culture of Klebs–Loeffler bacillus. At 3 p.m. of the same day she received 10 cc. of Behring's serum No. 2. The injection was made at the left lateral aspect of the abdomen. . . . About five minutes after the injection, the girl complained of tingling and became restless. . . . This paraesthesia was immediately followed by a slight general convulsion. This mild spasm was followed at once by general tonic and clonic convulsions, accompanied by marked opisthotonos, cyanosis and absolute cessation of breathing. The pulse was rapid, small and forcible. . . . Artificial respiration was kept up until the heart stopped. The time in all was perhaps three minutes from the first sensation of tingling till death.

An autopsy was performed eighteen hours after death by a coroner's physician, Dr. J. M. Clayland, whose report stated:

> Body well nourished. Rigor mortis well-marked. No oedema. There is a small punctured wound on the left side of the anterior abdominal wall. This puncture does not penetrate the peritoneal cavity, but in its course transfixes a small vein in the abdominal fat. The brain and meninges are congested. The liver, and especially the kidneys, are markedly congested. The lungs are normal. The heart is in systole; its left side is empty; the right side contains a small amount of fluid blood. There is slight atheroma of the aorta near the valves. The pulmonary artery contains no clots, and the larynx and trachea contain no foreign body.

As indicated by the photographic reproductions from the newspapers of the two periods (Fig. 2),

FIGURE 2.

each of these episodes created no small sensation in its respective community.

Both these patients stemmed from the same ancestry. The family has been traced to the beginning of the line on this side of the ocean and the relationships are shown in Figure 3.

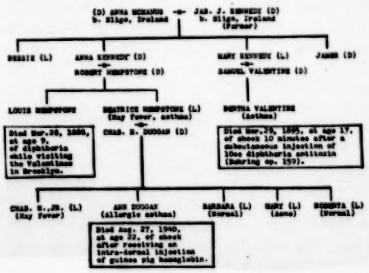

FIGURE 3.

The coincidence of two accidental deaths from allergic shock of young women in successive generations, although of divergent lines of the same

family, is so far as I know, unique in medical annals.

A detailed consideration of the influence of heredity in relation to allergy is beyond the scope of this paper. The cases reported here certainly show evidence of heredity sensitivity of high degree, transmitted through the females. The inheritance seemingly was not sensitiveness to species-specific antigens, unless a common antigenic fraction in horse, dog and guinea-pig proteins analogous to the Forssman heterophile antigen exists. A. D. had been shown to react to a variety of substances, and the passive-transfer test proved that she harbored reagins to both guinea-pig hemoglobin and dog hair but not to horse dander, while B. V.'s death was due to horse serum. The former had had definite exposure to a dog and her asthma had been greatly ameliorated by disposal of her pet Pekingese. But she had had no known contact with guinea pigs. It might therefore seem that she inherited a specific sensitivity as well as the capacity to become sensitized. Unfortunate for this as evidence is the probability that she had opportunities for sensitization to a guinea pig which would not necessarily have come to the knowledge of her relatives or even have been remembered by herself. It is thought that the evidence of these cases at least adds further support to the recognition of atopic persons as a distinct group in which a hereditary abnormality is the essential factor, and in which exposure to exciting substances is of secondary importance but determines the specificity of the antibodies (reagins) developed.

From the standpoint of liability to fatal reaction, A. D.'s case raises atopic hypersensitiveness to proteins of small animals to a clinical importance hitherto accorded to asthma and hay fever induced by contact with horses.

Sudden death as well as lesser effects, such as respiratory distress, collapse, pyrexia and local manifestations, including urticaria, hay fever and asthma, hypothetically result from the release of a physical irritant or a chemical poison produced by the clash (union) of antigen with antibody within the tissues of the body. That these toxic substances are of the nature of histamine is assumed by some, but their identity is as yet unknown. It is, however, well established that two definite effects, whatever the exact cause, are produced: smooth muscle is thrown into spasm, and permeability of the capillary walls is increased. These effects vary in promptness, severity and distribution according to various factors — dosage, time in relation to sensitization, the organ or tissue of the particular person in which antibodies predominate (individual shock organ) and, possibly, endocrine factors not yet identified but in which the thymus, lymphoid structures and adrenal cortex are under suspicion.

As in the case of other poisons that act with great speed or kill by altered physiologic functioning rather than by producing tangible structural lesions, the post-mortem findings are meager and not distinctive.

Evidence of smooth-muscle spasm may be furnished in the lung by overdistention of the air cells, often with breakdown of the alveolar walls. Such emphysematous lungs do not collapse when the chest wall is opened, but they do so slowly when incised. They are usually pale. The right side of the heart is usually distended and venous engorgement of the viscera is the rule. If death has not been too rapid, evidence of permeability of the capillaries may be shown by edema of the glottis and bronchial mucosa. Since death is asphyxial, subserous petechial hemorrhages are fairly frequent. Engorgement of the liver and portal system may be the outstanding feature. The lymphoid structures may be enlarged. The blood is fluid, and eosinophilia may be noted. Evidence of the "thymolymphatic constitution" such as characteristic bodily contours, abnormalities of thymus gland, and hypoplasia of the vascular system and adrenals may be seen. Hyperplasia of the germinal centers in the spleen and lymph nodes should be noted and checked by microscopical study. Finally, passive-transfer tests may determine the presence of specific reagins.

For establishment of a diagnosis of death from allergic shock the following criteria should, in my opinion, be fulfilled: there must be a definite history or tangible evidence of death in relation to the injection of an antigenic substance; the post-mortem findings must be consistent with death of this type, and exclude other adequate causes; antibodies or reagins specific to the substance known to have been injected must be demonstrated in the blood or tissues of the subject, or some clinical manifestation of an allergic reaction must have preceded death. A family or personal history of hypersensitiveness, if obtained, is pertinent and important but not essential.

The outstanding lesson of clinical importance to be derived from these cases is that of the ever-present danger attendant on the parenteral injection of any foreign proteid by an atopic person. Proteids capable of inducing fatal allergic shock are not limited to those derived from the animal kingdom. Lamson[3] has reported a fatality following the intradermal administration of 0.05 cc. of a 1:100 solution of extract of Bermuda grass,

and another from an intradermal skin test with a 1:500 solution of buckwheat extract, both in adults. Ziskind and Schattenberg[4] reported a fatality in an adult Negro woman from 0.2 cc. of antityphoid vaccine given intravenously to induce a nonspecific reaction in the hope of benefiting her arthritis. A first dose of 0.08 cc. four days previously had been given without reaction.

It is startling indeed that so minute a dose of foreign matter as was given in the first case, introduced barely under the epidermis of a seemingly healthy adult weighing 135 pounds, should have resulted in immediate death. Such an occurrence is not, however, without precedent, as the foregoing examples show. Cooke[5] in 1922 reported the death of a boy of three from a reaction to a skin test with a solution of glue. Lamson[6] in 1924 reported the case of a child with eczema who died two minutes after an intradermal test with 0.05 cc. of a mixed antigen containing egg albumin (0.1 mg. nitrogen per 1 cubic centimeter). Ferguson[7] has recently reported the case of a boy of six who received 0.18 cc. of antitetanus serum while under an intravenous anesthetic. It was given intradermally and death was preceded by development of a large wheal at the site of the injection. Boughton[8] gave 0.06 cc. of horse serum intravenously to an asthmatic patient, aged twenty-nine, who succumbed in forty-five minutes. Freedman[9] in 1935 reported a personal experience in which he gave a test dose of 0.05 cc. of horse serum intracutaneously to an asthmatic boy of six who had received an injection of diphtheria toxin-antitoxin at school twenty days previously. The child died in eight minutes despite vigorous treatment with adrenalin and artificial respiration.

Although injection of the foreign proteid in most of the fatal cases has been by the subcuticular or the intravenous route, my experience, Freedman's and Ferguson's cases and some of those collected by Lamson[6] show definitely that the intradermal route may be just as dangerous to the hypersensitive person. For this reason, conjunctival or scratch tests are preferred. If the intradermal method is necessary, maximum precautions should be observed. The problem of treatment by serum of a hypersensitive person belongs to the skilled specialist in immunology quite as truly as resection of the stomach belongs to the skilled surgeon.

In this connection a comment by Rackemann[10] bears repeating: "It is certainly true that where the degree of sensitiveness is exquisite, minute amounts of foreign serum are all that are required to produce a fatal reaction. The possibility of producing them in one case justifies the greatest caution in treating a hundred others."

To the clinician who is faced with the need to administer serum and wishes to do so with maximum safety, the recent paper by Rackemann[11] and the dicta laid down by Fantus and Feinberg[12] in 1936 are recommended. Several excellent textbooks[13–15] are also available.

Inasmuch as transfusions are becoming increasingly common and blood banks are springing up all over the country, it seems advisable in the present state of our knowledge to exclude as blood donors the atopic allergic persons, especially those who are sensitive to horses. This advice is based on the classic experience of Ramirez[16] of the unintentional passive transfer of horse asthma to a patient by a transfusion from an asthmatic person.

What has been said of precautions in relation to hereditary hypersensitive persons applies with almost equal force to that not inconsiderable portion of the population who may have been artificially sensitized by previous administration of serums, although the liabilities in this group are less grave.

Summary

A recent case of sudden death from an intradermal injection of a minute amount of guinea-pig hemoglobin is reported. This case is correlated with that of the first case in this country of death from diphtheria antitoxin, and the familial hypersensitiveness affecting both is revealed.

The autopsy findings in both cases are stated, and attention is again called to the value of the Prausnitz–Küstner test as a post-mortem procedure.

Persons hypersensitive to the proteids of small animals are put in the same category as those who are sensitive to horses so far as the dangers of foreign-proteid therapy are concerned. Use of the intradermal route for preliminary testing is discouraged.

Meticulous observance of appropriate precautions in parenteral therapy by antigenic substances is urged.

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TECHNICAL CONSIDERATIONS IN EXCRETORY UROGRAPHY

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THIS study of 200 cases was undertaken to determine, if possible, the best preparation of patients for excretory urography. It is essential that one obtain clear films, unobscured by gas and fecal material, if plain scout films of the abdomen (kidney, ureter and bladder areas) and excretory urograms are to be of diagnostic value. If the blood urea is above 70 mg. per 100 cc., it is unlikely that the kidneys will be able to excrete enough of the radiopaque medium in the concentration necessary to outline adequately the kidney pelves, ureters and bladder. Good visualization of the kidney pelvis in the film taken five minutes after the injection of the radiopaque medium generally denotes good function of that kidney, although the reverse is not always true.

Each of the 200 patients in this series received intravenously 20 cc. of Neo-Iopax (*di*sodium *N*-methyl-3, 5-*di*iodo-4-pyridoxyl-2, 6-*di*carboxylate). No patient experienced vomiting, arm cramps or unpleasant symptoms, although a few complained of a feeling of warmth and slight nausea; these symptoms were readily alleviated by taking a few deep breaths. The absence of unpleasant symptoms can be attributed to four factors; the radiopaque medium employed, reassurance of the patient before the injection, the precaution of making certain that the 20-gauge short bevel needle was well within the lumen of the vein before the injection was begun and deep breathing by the patient immediately after the injection. Although it is generally recommended that the radiopaque medium be injected slowly, I found no correlation between the speed of the injection and the production of untoward symptoms. Furthermore, I have been unable to demonstrate the value of using an abdominal compression band or balloon in excretory urography, although in an occasional case a 5 to 10° Trendelenburg position may be of some value in obtaining a better filling of the kidney pelves.

There was no uniformity of preparation in this series, since the patients were referred from various sources. This very lack of uniformity and the necessity of obtaining data concerning the preparation of each patient led to a study of the various resulting preparations and the time relation between the ingestion of food, the taking of water, castor oil and enemas and the making of the roentgenograms.

In each patient a plain scout film of the abdomen (kidney, ureter and bladder areas) was taken, the radiopaque medium was injected, and films were taken routinely five, twenty and forty-five minutes after the injection. Each film was developed immediately. Delayed, upright and oblique films were taken as indicated by a careful observation of the wet films.

In patients with hypertension a three-minute film is imperative after the injection, because observation has revealed that the kidneys excrete the radiopaque medium very rapidly in the majority of these cases, so rapidly, in fact, that all the radiopaque medium, for reasons unknown, may be in the bladder within five minutes after the injection.

The excretory cystograms obtained should be studied carefully, for valuable diagnostic information may be revealed in regard to prostatic hypertrophy, diverticulums, nonradiopaque stones, extravesical pressure, tuberculosis "splinting" and tumors. An estimate of the residual urine, as well as information regarding the emptying of a diverticulum, if present, may be obtained by taking another film of the bladder area after the patient has voided.

In accident cases suspected of having a ruptured kidney, ureter or bladder, excretory urograms should be taken within two hours, if possible, because the intestines of these patients rapidly become distended with gas, which may interfere with adequate visualization of the lesion.

In this particular series, I avoided the use of Pitressin because of the unpleasant symptoms that

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not infrequently result from its use. In carefully selected cases, its use is recommended.

The correlation between methods of preparation of the patient and the resulting plain scout films of the abdomen and excretory urograms is shown in Table 1. The films were graded as satisfactory or unsatisfactory from the point of view of radiographic clearness and detail.

TABLE 1. *Results of Preparation for Excretory Urography.**

Group No.	No. of Cases	Type of Preparation	Results: Percentage of Satisfactory Preparations	Results: Percentage of Unsatisfactory Preparations
1	23	No preparation	52	48
2	22	Castor oil at 7 p.m.; no enema	95	5
3	75	Castor oil at 7 p.m.; enema at 7 a.m.	53†	47
4	37	No castor oil; enema at noon	59	41
5	5	Castor oil at 7 a.m.; no enema	80	20
6	38	Castor oil at 7 a.m.; enema at noon	89	11

*All the scout films and urograms were taken in the afternoon except in Group 2, in which they were taken in the morning.

†Seventy-seven per cent of scout films taken in the morning were satisfactory.

A study of the table reveals that the smallest number of satisfactory plain scout films of the abdomen and excretory urograms were obtained in patients who had no preparation (Group 1), who had 30 cc. of castor oil at 7 p.m. and a soapsuds enema at 7 a.m. (Group 3) and who had only an enema (Group 4). Plain scout films of the abdomen were made in the morning on all 75 patients in Group 3, and these were repeated in the afternoon immediately prior to the taking of the excretory urograms. Whereas 77 per cent of scout films of the abdomen taken in the morning were satisfactory, by afternoon only 53 per cent of the scout films and urograms were satisfactory, because the intestines in the interim had ballooned out with flatus, apparently owing to atony following the prolonged spasm produced by the castor oil.

Practically all the unsatisfactory scout films and excretory urograms were the result of flatus in the intestines. Enemas alone increased flatus, although if 30 cc. of castor oil had been taken the enemas caused less flatus because the castor oil apparently aided in expelling the air and water introduced with the enema. Another factor to be considered is that enemas may also interfere with the desired dehydration of the patient before excretory urography. Bed patients are difficult subjects to prepare satisfactorily for plain scout films of the abdomen and excretory urograms because of intestinal flatus, for rest in bed is not conducive to good gastrointestinal tone.

In groups receiving the same preparation in regard to castor oil and enemas, the best plain scout films of the abdomen and excretory urograms were obtained in the patients whose fluid intakes had been restricted to 250 cc. for the previous eight hours and who had not had a meal prior to the taking of the roentgenograms, while the poorest results were obtained in the patients who had eaten nothing for twenty-four hours. For reasons of brevity, the data substantiating these conclusions have been omitted.

Reference to the table shows that, other things being equal, the best results followed the oral use of castor oil alone (Groups 2 and 5), or castor oil followed in five to twelve hours by a soapsuds enema, provided that the roentgenograms were taken not later than fourteen hours after the administration of castor oil (Group 3 — morning films — and Group 6).

Summary

Factors conducive to the obtaining of satisfactory plain scout films of the abdomen and excretory urograms are evaluated in 200 cases.

It is concluded that castor oil alone and castor oil followed by a soapsuds enema in five to twelve hours, provided the films are taken within twelve hours after the administration of the castor oil, produce the most satisfactory results. Furthermore, fluids should be restricted for eight hours prior to taking the films, and an immediately preceding meal should be avoided.

MEDICAL PROGRESS

PROPHYLAXIS IN RHEUMATIC FEVER*

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A SPECIFIC agent for the prevention of rheumatic fever will probably not be available before the cause of the disease is known. Until that time, efforts directed toward prophylaxis must consist of general measures that have emerged from gradually accumulated knowledge concerning certain underlying and precipitating factors in the disease. It is obviously desirable to prevent the initial attack of rheumatic infection but, for practical purposes, efforts must be directed mainly toward the prevention of recurrences in patients known to be susceptible to rheumatic infection by virtue of previous attacks. If it were possible to separate the susceptible from the nonsusceptible by some simple test, such as the Dick or Schick test, the prevention of initial attacks might become possible.

The most widely held and best-supported view of the pathogenesis of rheumatic fever at the present time is that certain persons, because of hereditary or environmental factors, or both, have developed abnormal tissue reactions to hemolytic streptococci. The prevention of rheumatic attacks, therefore, is based largely on the prevention of hemolytic streptococcus throat infections.

Maintenance of proper nutrition and avoidance of fatigue and chilling are primarily aimed at increasing the patient's general resistance to infection. Of first importance is education of the patient and his family concerning the role of respiratory infections in rheumatic attacks and the strict necessity for protecting rheumatic subjects against such infections so far as possible. There is much to be said, from this point of view, in favor of special school classes for rheumatic children, where there is careful supervision, those in charge understand the problems involved, and the children are segregated from the general school population. In many parts of the country, rheumatic fever is a more pressing public-health problem than such diseases as tuberculosis and typhoid fever, yet no measures have been devised or undertaken to control the spread of what appears to be a highly important precipitating agent in rheumatic fever — hemolytic streptococcus infection.

Hubbard and Griffin[1] instituted open-air sanatorium care for rheumatic children with the view of diminishing exposure to hemolytic streptococci. Bacterial counts of the air in the pavilions revealed few pathogenic organisms. At the beginning of the study 20 children with recent, but clinically inactive, rheumatic fever were admitted. There were no new admissions during the year. Visitors wearing masks and free of respiratory infection were allowed in the wards only once a week. None of the 20 patients developed respiratory infections or rheumatic activity. After returning home in excellent health their resistance to rheumatic fever appeared to continue. In addition to supplying confirmatory evidence of the relation between respiratory infection and rheumatic activity, the results also suggest that when the disease has become thoroughly quiescent, and not just subclinical, recurrences are less likely to occur. The prolonged treatment of an attack may thus become a safeguard against future exacerbations. It is to be hoped that further follow-up studies will be forthcoming.

HEREDITY

Wilson[2] has gathered evidence that susceptibility to rheumatic fever is transmitted as a single autosomal gene, and has compiled a table of prediction of the probable occurrence of rheumatic fever in the progeny. According to this table, if both parents have a positive history of rheumatic infection, nearly all progeny will become afflicted. If one parent is positive and a grandparent on the other side of the family is positive, the expected incidence in the progeny is about 50 per cent. If both parents are negative but one grandparent of each line is positive, the expected incidence is about 25 per cent. Although this knowledge is not likely to provide a fruitful field for the prevention of rheumatic infection, it should be kept in view in advising patients on the subject of marriage and childbearing. In any event, the offspring of families in which rheumatic fever is prevalent should be under close observation in order to detect the disease at its onset.

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*. Volume III. 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942. $5.00).

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Climate

At one time streptococcal infections and rheumatic fever were thought to occur rarely in tropical and subtropical climates. In recent years this has been repeatedly refuted.[3-6] There is, however, evidence that rheumatic fever is much less frequent and usually milder in the southern United States than in the northern temperate zone. Nichol[7] found that rheumatic heart disease was only one third as frequent in native-born children in southern Florida as in children born in the northern states but residing in the South. Bailey[8] believes that the disease is definitely milder in the South. He found that of a group of 42 children with illness ascribed to rheumatic infection, only 30 per cent developed signs of valvular damage, and in most of these the signs were minimal. Paul and Dixon[9] studied the incidence of rheumatic heart disease in Indian children, and found that in the northwestern states 4.5 per cent of the children had signs of rheumatic heart disease, whereas in the southwestern states the incidence was only 0.5 per cent. The authors considered that all Indians are essentially similar in racial background, social and economic status and habits of hygiene, so that this striking difference must be attributable to the more equable climate in the Southwest. Several years ago Coburn[10] transported 10 children with stubborn rheumatic infection from New York to Puerto Rico. The infection quickly became quiescent and remained so while the children resided in the tropics, but reappeared as soon as they returned to New York. Nichol[7] was also impressed with the rapid subsidence of rheumatic infection in children transported from the northern states to southern Florida. Jones et al.[11] were less enthusiastic concerning their experience with transporting 26 rheumatic children from Boston to a subtropical climate. Whereas some of their patients did well, others continued to have active infection. Three died while in the South, and 2 others showed increased activity of the infection.

It is clear that transportation to southern climates is not the answer to the problem of rheumatic infection, not only because the disease may recur or remain active in such climates, but also because the economic status of the majority of rheumatic patients prohibits such migration. When permanent residence in tropical or subtropical climates can be arranged without hardship or financial sacrifice, it appears to be a reasonable prophylactic undertaking. However, there is the danger that such a move will produce a false sense of security and neglect of other more effective prophylactic measures. The evidence at hand indicates that it is better for the patient to remain in the North and receive sulfonamide prophylaxis (see below) than to move to the South and receive no chemoprophylaxis.

Tonsillectomy

The relation between tonsillitis or pharyngitis and rheumatic infection has been noted for years. It seemed only reasonable to suppose that tonsillectomy might reduce the incidence of throat infections and, hence, rheumatic manifestations. Early statistical studies seemed to support such a thesis but, as emphasized by Wilson, Lingg and Croxford,[12] the age at operation, the period of observation and the inclusion of suitable controls are factors of importance sometimes neglected in such studies. These authors found that the incidence of initial attacks or recurrences was not significantly different in tonsillectomized or nontonsillectomized children. Recurrences were frequent in both groups under the age of nine years and less common in older children, irrespective of the presence or absence of the tonsils. Subsequent careful surveys[13-17] have, on the whole, confirmed the absence of any striking beneficial effect of removal of the tonsils on the course of rheumatic fever.

In 1936, Kaiser[18] reported the results of statistical analysis of a large group of children, which indicated that tonsillectomized children are somewhat less likely to develop rheumatic fever than nonoperated children and that the disease is severer in nontonsillectomized patients. He found the mortality rate to be nearly twice as high in children whose tonsils were present at the time of the initial attack. He concluded that statistical and clinical data justify the removal of tonsils in practically every rheumatic child, even though his figures did not indicate that the incidence of recurrences was favorably influenced by tonsillectomy. Furthermore, the difference in mortality rates was apparently dependent on removal of the tonsils in anticipation of the initial rheumatic attack. In 1940, Kaiser[19] reaffirmed his opinion that fatal carditis is noted less frequently in tonsillectomized than in nontonsillectomized children.

The problem is an extraordinarily difficult one, not only because of the many variable, and often hidden, factors that affect the course of rheumatic fever, but also because of the more obvious, and neglected, factors of incomplete removal of the tonsils and of hypertrophy of the pharyngeal lymphoid tissue that commonly follows removal and that may serve as a focus of infection as effectively as do the tonsils themselves. The bulk of evidence at present is certainly opposed to the routine removal of tonsils because of rheumatic

susceptibility. All students of the problem are agreed that tonsillectomy should be performed in rheumatic patients when local conditions exist that are thought to indicate removal of the tonsils in nonrheumatic patients. There is also general agreement that the operation should be performed only after the infection has become quiescent, since otherwise an acute exacerbation may result.

Vitamin C

One of the predisposing factors in rheumatic infection has appeared to be undernutrition, and of the various essential foodstuffs, vitamin C has attracted the widest attention. Rinehart[20] studied the pathologic lesions produced in guinea pigs maintained on an inadequate intake of vitamin C and infected with virulent bacteria. Lesions were thus produced in heart muscle, valves and joints, and subcutaneous nodules were formed that were similar to the lesions found in rheumatic fever. Most of the experiments were done with the hemolytic streptococcus, but this organism had no specific effect, since identical lesions were produced by other types of bacteria. In the presence of adequate vitamin C intake, infection with the same organisms did not produce the "rheumatic" lesions. In a subsequent study of plasma ascorbic acid levels, Rinehart, Greenberg, Olney and Choy[21] found that in both active and inactive rheumatic fever there was usually an abnormal level and that, on the average, the level was lower than in a group of patients with miscellaneous infections. They postulated that the deficiency might be brought about by inadequate intake (namely, poverty), depletion by the disease or inherent metabolic fault.

Soon after the appearance of the reports on the experimental results in guinea pigs appeared, many investigators[22-26] were led to try the effects of large doses of ascorbic acid on patients with rheumatic fever. The results were universally discouraging from both the prophylactic and the therapeutic point of view. Meanwhile McBroom, Sunderland, Mote and Jones[27] repeated the guinea-pig experiments and found that acute scurvy alone produced the same lesions that had previously been ascribed to chronic vitamin C deficiency and infection. The authors suggested that the diet used in the experiments of Rinehart permitted only moderate deficiency, and that the superimposed infection simply made the deficiency complete.

All observers are agreed that it is desirable to maintain adequate intake of all essential foodstuffs, but there are no data indicating conclusively that large amounts of vitamin C or any other food substance have any specific beneficial action in the prophylaxis or treatment of rheumatic infection.

Sulfonamide Prophylaxis

It has long been known that tonsillitis or pharyngitis frequently precedes an attack of rheumatic fever, and bacteriologic study of the offending organism has implicated Group A hemolytic streptococci. It has also been demonstrated by immunologic methods (antistreptolysin, antifibrinolysin, precipitin and agglutinin reactions) that most patients with rheumatic fever are suffering from either active or recent hemolytic streptococcus infections. It was only natural to hope that the sulfonamides, known to be effective against the streptococcus, might prove to be useful in the treatment of rheumatic fever. Unfortunately this was a false hope, for not only was sulfanilamide ineffective in the treatment of the disease, but patients were often made worse by the drug.[28, 29] Toxic reactions with high fever were commonly seen, and congestive heart failure was not infrequently precipitated. Whether this latter effect was due to the toxic reaction, to the intensification of the rheumatic state or to a myocarditis produced by the sulfonamides[30] is not clear, but it soon became apparent that the drug was ineffective in combating the rheumatic infection, and that it was equally ineffective in preventing rheumatic manifestations if administered at the time of pharyngitis or tonsillitis due to the hemolytic streptococcus.[28, 29, 31, 32]

The possibility of preventing hemolytic streptococcus throat infections by the administration of small doses of sulfanilamide over long periods of time to patients susceptible to rheumatic infection was then investigated, and reports by Coburn and Moore[32] and by Thomas and France[33] appeared in 1939. Coburn and Moore[32] administered sulfanilamide in doses of 2 gm. a day to 80 rheumatic patients during the winter and spring seasons, and only 1 of these developed hemolytic streptococcus infection and signs of rheumatic activity. The results of Thomas and France were equally encouraging, despite the use of smaller doses of sulfanilamide (1.0 to 1.3 gm. a day). They reported their results on 30 patients treated for two winter and spring seasons and included 30 control patients of approximately the same ages. In the treated group there were no major rheumatic episodes, whereas in the control group five such episodes occurred. Two minor attacks took place in both groups and, in addition, there were three questionable attacks of rheumatic fever in the control group. Important toxic reactions were not encountered by either group of investigators. In 1940, Coburn and Moore[34] reported on

a group of 184 subjects treated prophylactically with sulfanilamide, with an incidence of rheumatic attacks of less than 1 per cent, instead of the usual rate of 35 per cent.

Thomas, France and Reichsman[35] used sulfanilamide prophylactically in 55 patients. There were no serious toxic reactions and no patient developed a major attack of rheumatic fever. In a control group of 67 patients there were fifteen major attacks of rheumatic infection. The choice of control patients in earlier studies had been criticized on the ground that many of them had been placed in the control group because of indifference to the disease and an unwillingness to make the frequent visits necessary to the study. Such patients obviously might be expected to do less well irrespective of the use of sulfanilamide. Actually, Thomas, France and Reichsman found that the number of attacks was somewhat less in the unco-operative control group than in those patients who were placed in the control group for reasons other than unco-operativeness.

Coburn and Moore[36] presented a follow-up report on patients who had previously received sulfanilamide prophylactically. It occurred to them that the previously reported favorable results might have been due, at least in part, to the increasing age of their patients, with consequent diminution in susceptibility to recurrences. During 1939–1940, therefore, 100 patients who had received prophylactic treatment with sulfanilamide from 1936 to 1939 were taken off the drug. In this group 32 developed hemolytic streptococcus pharyngitis, and of these 40 per cent developed a recurrence of rheumatic fever. This follow-up study demonstrated that the rheumatic children who escaped while receiving sulfanilamide were still susceptible, when untreated, to streptococcal infection and rheumatic fever.

Stowell and Button[37] observed toxic effects of sulfanilamide in 19 of 46 patients treated prophylactically. In 25 per cent the drug was stopped permanently on account of rash, fever, nausea or lowering of the leukocyte count. One child died of agranulocytosis after twenty-nine days of sulfanilamide prophylaxis. The dosage was of the same order as that used by other investigators, that is, from 1.5 to 2.0 gm. a day in divided doses. The authors felt obliged to give up the prophylactic use of sulfanilamide because of the high incidence of toxic reactions, although they too reported fewer rheumatic recurrences in those who were able to tolerate the drug. Stowell and Button's report seems unduly pessimistic toward this form of therapy in the light of the accumulated experience of other investigators. Thomas[38] collected a series of rheumatic persons treated for 648 patient-seasons, made up of her own cases and those of others, reported and unreported. The death reported by Stowell and Button was the only serious toxic reaction in this large series, whereas the prophylactic effects were excellent. There were only six rheumatic recurrences in the entire group — less than 1 per cent instead of the expected rate of approximately 30 per cent. Since then, Hansen, Platon and Dwan[39] have reported an additional 78 patient-seasons with only one recurrence (actually two recurrences, but one of these occurred six days after the beginning of sulfonamide therapy and should not be classed as a prophylactic failure). Toxic manifestations were seldom encountered, although in 1 case sulfonamide was discontinued when the leukocyte count dropped to 1700.*

There can be no doubt that prophylaxis of rheumatic fever with the sulfonamides is an important advance in the control of rheumatic fever. If patients receiving the drug are followed carefully, the incidence of toxic reactions of serious degree will certainly be far less than the mortality and morbidity of active rheumatic infection. Although the initial studies included a large variety of laboratory tests, experience has shown that, for practical purposes, prophylaxis may safely be carried on with frequent determinations of the hemoglobin level and the leukocyte count and an occasional test to the sulfonamide blood level. A number of observers have noted a gradual lowering of the leukocyte count during the first weeks of treatment with sulfanilamide, sometimes to levels as low as 2500, with a subsequent increase to normal without discontinuance of the drug. At such times the granulocytes may fall to 25 or 30 per cent.[38] In the event that such a fall does occur, daily leukocyte counts should be made and the drug discontinued if the count falls below 2000.

According to Thomas,[38] the drug should be begun before discharge of a patient following an attack of rheumatic fever because of the danger of exposure to respiratory infections in the home. The temperature and leukocyte count should be normal after withdrawal of salicylate, but there is no need to wait for the erythrocyte sedimentation rate to return to normal. Thomas further advocates that prophylaxis be continued throughout the year rather than for the winter and spring seasons only, since not a few recurrences come in the summer and fall, and that prophylactic sulfonamide be administered for five years or longer after an attack of rheumatic fever.

*Since this manuscript was prepared, Kuttner and Reyersbach[40] have reported on sulfanilamide prophylaxis in 108 patient-seasons with only one rheumatic recurrence. This brings the total reported patient-seasons to 834 with only eight rheumatic episodes instead of the expected rate of approximately three hundred rheumatic attacks. These authors report toxic manifestations in about 15 per cent of subjects receiving sulfanilamide.

Up to the present, sulfanilamide has been the chemoprophylactic agent reported on. In many clinics some of the less toxic sulfonamides, especially sulfadiazine, are now being evaluated. There is little reason to doubt that toxic reactions will be less troublesome, and no reason for supposing that sulfadiazine will prove to be less effective than sulfanilamide. In a small group of children treated prophylactically with sulfadiazine at the Massachusetts Memorial Hospitals for the past two years, the drug has been discontinued in only 1 case because of toxic reaction (rash and fever), and there has been no lowering of the leukocyte count during the early weeks of chemoprophylaxis such as has been observed with sulfanilamide. The number of subjects treated is too small to allow comparison of the effectiveness of sulfadiazine and sulfanilamide, but our experience suggests that sulfadiazine will prove to be more effective than sulfanilamide only in so far as a better tolerated drug will benefit more patients.

Salicylate Prophylaxis

Following the demonstration by Derick, Hitchcock and Swift[41] that aspirin (or neocinchophen) usually prevented the arthritis of serum sickness and that, in patients so treated, the production of precipitins against horse serum was inhibited, several investigators were led to try the effects of aspirin in the prevention of rheumatic fever. Leech[42] treated 65 children with inactive rheumatic heart disease or potential heart disease with 20 gr. of aspirin daily for six months. Seventy-nine children served as controls. Definite rheumatic recurrences occurred in 7 per cent of the treated group and in 11 per cent of the control group. This is hardly a significant difference but, in addition, the author reported that the children who received aspirin enjoyed better general health, gained more weight and had fewer minor complaints than those who did not. Sheldon[14] was not convinced that a course of aspirin begun at the time of onset of pharyngitis was definitely beneficial, but admitted that it deserved further trial. Perry[43] administered aspirin in 10-gr. doses three times a day for twelve months to 41 rheumatic children. Recurrences occurred in 12 per cent of the treated group and in 18 per cent of a control group. Perry considered the difference insignificant, and attributed the better general health of the treated children to the fact that the parents of children receiving continuous medication of any kind are likely to be more attentive to details than the parents of children receiving no medication. Schlesinger[44] gave 7 to 12 gr. of aspirin three times a day at the onset of pharyngitis in rheumatic children. He reported fewer rheumatic recurrences in children so treated and a much milder illness in those in whom recurrences did occur.

Coburn and Moore[45] administered sodium salicylate in doses of 60 to 90 gr. daily for one month to rheumatic subjects who developed pharyngitis and in whom Group A hemolytic streptococci were cultured from the throat. No patient with pharyngitis without this group of organisms received salicylates and none developed rheumatic fever. Forty-seven quiescent rheumatic subjects were given salicylates at the onset of hemolytic streptococcus pharyngitis, of whom only 1 developed rheumatic fever. Fifteen other patients showed a brief asymptomatic rise in the erythrocyte sedimentation rate after the withdrawal of salicylates. As a control group, 139 untreated rheumatic subjects with Group A hemolytic streptococcus pharyngitis were observed; of these, 57 developed recurrences of rheumatic fever. Coburn and Moore do not describe the nature or severity of the recurrences that appeared in the control group, and if one considers the 15 treated patients with elevated sedimentation rates as having mild, partially masked recurrences, the incidence of attacks was equal in both groups. It is probably safe, however, to assume that the difference in the two groups was impressive and significant, for these authors are well aware of the vagaries of rheumatic fever. It is of some interest that the titer of antistreptolysin was unaffected by salicylates, being essentially the same in both series of patients.

Vaccine Prophylaxis

Small[46] isolated a nonhemolytic streptococcus from the blood and throats of patients suffering from rheumatic fever that he considered to be the etiologic agent and with which he prepared a vaccine and an antiserum. He reported that both appeared to be of benefit in the treatment of patients with rheumatic fever. Swift, Hitchcock, Derick and McEwen[47] isolated a streptococcus labeled "Strain Q33" from the tonsillar exudate of a patient with severe rheumatic fever and prepared a vaccine. In accordance with the view that rheumatic fever represents a hypersensitive reaction to streptococci and that animal experiments indicate that subcutaneous injection of antigen tends to sensitize, whereas intravenous injection diminishes, tissue reactivity, the authors administered this vaccine intravenously in gradually increasing doses. Although very cautious in their claims, they believed that the results were encouraging. At the same time, Wilson and Swift,[48, 49] using the same vaccine, reported a decrease in the number of recurrences of rheumatic fever in vaccinated children. Of the vaccinated group 45 per

cent remained free of recurrences for sixteen to twenty-four months, but only 18 per cent of the control series remained free of rheumatic fever. Later, however, Wilson, Josephi and Lang[50] were able to show equally good results with small doses of typhoid vaccine, so that improvement was either fortuitous or due to a nonspecific stimulation of resistance. These authors were led to the conclusion that vaccination with the various antigens used did not influence the incidence of rheumatic recurrences.

Coburn and Pauli[51] immunized 52 nonrheumatic members of a nursing class (an equal number of subjects in the same class served as controls) with streptococcus toxin (Strain NY 5), beginning with 500 S.T.D. (skin-test doses) and gradually increasing the dose to 80,000 S.T.D. Each subject received between 300,000 and 400,000 S.T.D. The authors found no evidence that the course of immunization increased resistance to streptococcal infections or rheumatic fever. Wasson in 1933 began experiments on the immunization of rheumatic subjects with a filtrate made from Strain NY5. In 1938, she[52] reported apparently beneficial effects in 34 subjects immunized with gradually increasing doses of vaccine administered subcutaneously. In 1940, Wasson and Brown[53] reported an incidence of rheumatic attacks in 10 per cent of immunized subjects, whereas in the control group recurrences occurred in 44 per cent. Unfortunately, the patients in the treated series were on the average four years older than those in the control group, that is, 12.9 years for the treated and 9.0 years for the controls. This factor alone may well have accounted for some of the difference in the incidences of rheumatic attacks. Another group of immunized children reported in the same communication[53] showed a similar diminution in the number of rheumatic recurrences, but again the treated patients were on the average older than the controls.

Wasson and Brown further reported follow-up observations on subjects previously immunized and found an incidence of rheumatic attacks in 7 per cent of patients previously immunized, whereas the incidence in the control group was 33 per cent. The average age in the latter series was actually slightly higher for the control group, being 12.0 years for the patients and 12.6 years for the controls. The authors thought that this indicated benefit after the cessation of the immunization program, but admitted that the control group was made up of unco-operative patients and that indifference to the disease might well have affected their general health and care. Recently the same authors[54] reported another series of immunized rheumatic subjects. Of 43 patients treated during 1939 and 1940, only 7 per cent developed rheumatic attacks, whereas in a group of 45 control patients the incidence of attacks was 40 per cent. In this series the average age of the treated and the control group was the same. During 1940 and 1941 the incidence of rheumatic attacks was 11 per cent in the treated and 33 per cent in the control group. As in the previous reports, follow-up studies showed continued benefits after cessation of the immunizing course.

Wasson and Brown also reported on the results of a modified and shortened course of immunization. A tannic-acid-precipitated toxin of Strain NY 5 was given intradermally in four injections of 5000, 8000, 10,000 and 12,000 S.T.D. at three-week intervals, following which 10,000 S.T.D. was given every six months. Forty-two subjects were so immunized, and during a nine-month period of observation there were no rheumatic attacks, whereas in 33 controls the incidence of attacks was 33 per cent. The average age for the treated group was 10.9 years, as compared with 12.1 years for the controls. If these results are confirmed, the procedure of immunization will be about as effective as sulfonamide prophylaxis and, in addition, will have the advantages of economy, safety and convenience. More investigation on the subject should be done, but in view of the unfavorable experience of Coburn and Pauli,[51] using a vaccine prepared from the same strain of streptococcus, it is doubtful that such hopes will be realized.

29 Bay State Road

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29161

PRESENTATION OF CASE

A thirty-year-old salesman was referred to the hospital by his company physician because of a mass in the region of the upper lobe of the right lung.

Five days prior to admission an abnormal mass was found in the upper right-lung field in a chest plate taken as part of a routine physical examination. The patient was not subjectively ill and had no complaints. There was no dyspnea, orthopnea, palpitation, pain, cough, hemoptysis, fever, chills, night sweats, asthenia, fatigability or weight loss.

One week before entry the patient had contracted an upper respiratory infection with an associated moderate watery nasal discharge and a nocturnal cough productive each morning of a small amount of yellowish sputum. This cleared completely after four days without sequelae. The family and past histories were noncontributory.

Physical examination revealed a well-developed and well-nourished man who appeared comfortable. Several small (3 to 4 mm.), soft, movable, epitrochlear lymph nodes were palpable on the right side. The pupils were equal and round and reacted to light and accommodation. There was slight narrowing of the isthmus of Krönig on the right and questionable dullness to percussion at the right apex anteriorly, where the breath sounds were louder than on the left. The heart and abdomen were normal. Six to eight pea-sized yellow, subcutaneous nodules were felt in the scrotal skin. Rectal examination was negative.

The blood pressure was 130 systolic, 80 diastolic. The temperature, pulse and respirations were normal.

The red-cell count was 4,200,000, with a hemoglobin of 15 gm., and the white-cell count 7300, with 71 per cent polymorphonuclear neutrophils. The urine was normal. A blood Hinton test was negative.

A chest roentgenogram revealed a sharply rounded area of increased density measuring 8 by 10 cm. and lying in the posterior aspect of the right chest and extending to the apex (Fig. 1). Fluoroscopically the mass seemed to move with respirations but not with swallowing. The right fourth rib was deformed. The chest was otherwise not unusual. In x-ray films of the dorsal spine the mass seemed to lie in the posterior mediastinum. The posterior aspects of the third and fourth ribs on the right side were spread, and there was a suggestion of erosion of the lower aspect of the third and the upper aspect of the fourth rib. The upper dorsal vertebras showed no definite evidence of pressure defect. The neural canals were not visible.

On the eighth hospital day a thoracotomy was performed.

DIFFERENTIAL DIAGNOSIS

DR. RALPH ADAMS:* Perhaps we had better see the x-ray films first.

DR. LAURENCE L. ROBBINS: This is an excellent demonstration of the smooth homogeneous mass, which is located in the right upper-lung field. From its position I should say that it arises from the posterior mediastinum, although in the lateral view the lower bulge of the tumor seems to be in the midportion of the chest. There is definite separation of the ribs and apparent erosion. However, I think the entire fourth rib is abnormal. Otherwise the chest appears normal.

DR. ADAMS: The differential diagnosis for a lesion at the thoracic inlet requires three processes of deductive reasoning, based on the available data. First, one considers the anatomic sites from which the disease might originate, they being in this case the lung, the pleura, the neck and the mediastinum. Second, one enumerates the possible diseases for each site of origin, in this instance including tuberculosis and tumor for the lung, empyema for the pleura, a substernal thyroid gland and thymoma for the neck, and an esophageal tumor, aneurysm, embryonic arrest and neurogenic tumor for the mediastinum. Third, one analyzes the likelihood of each possibility as substantiated or negated by subjective and objective evidence.

Tuberculosis or tumor of the lung is unlikely because there had been no cough, sputum, hemoptysis or pain, the mass was encapsulated and lay medial to the lung, and there were no x-ray shadows indicative of change within the lung parenchyma.

Any area of encapsulation within the thorax and outside the lung may represent empyema, but if of this size, preceding fever or malaise would have been a part of the history. Furthermore, empyema of sufficient size and duration to cause rib erosion cannot exist without accompanying periostitis visible by x-ray, and evidence of periostitis is not seen on these films.

*Surgeon, Lahey Clinic.

The possibility that a substernal or plunging goiter arose in the neck is excluded by the absence of a palpable neck mass and by the lack of deviation or compression of the trachea. The thyroid trachea begins near the hyoid cartilage and extends downward in a smooth arc, and the deviation is maximal at the greatest diameter of the thyroid tumor. By virtue of these facts one can anticipate

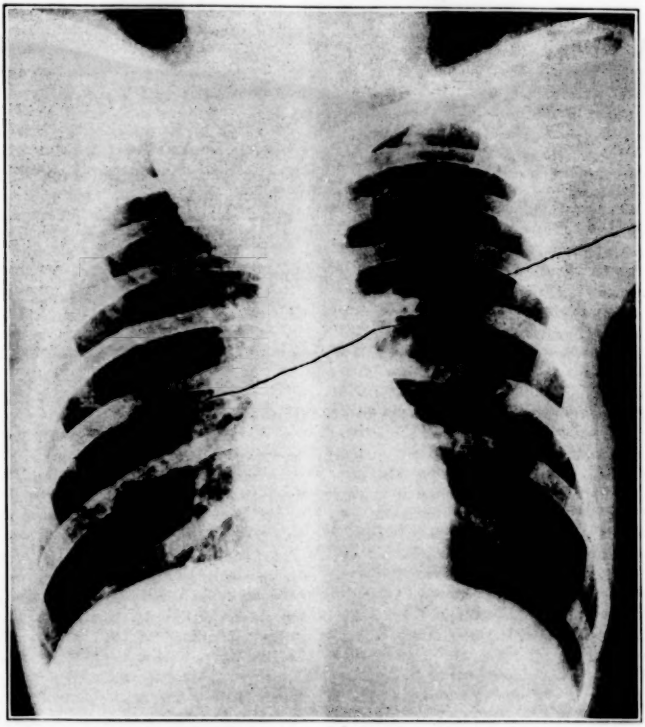

FIGURE 1. *Roentgenogram Showing Mass in Right Upper Mediastinum.*

gland is mentioned in the differential diagnosis of this case only because it must be considered whenever one is confronted with a unilateral upper mediastinal encapsulated mass. To gain access to the mediastinum, the thyroid gland must overcome the resistance of the first rib if it descends laterally, or the spine and manubrium if it descends anteriorly or posteriorly to the trachea. The disproportionate bony resistance always causes alteration of the tracheal contour, or at least there has been no exception to this statement in one large series of intrathoracic goiters. Two further facts may be of passing interest in relation to tracheal displacement caused by thyroid enlargement, as they are often of differential value. The curvature of the

the technical problems to be solved in the removal of a subclavicular or substernal goiter.

Since there were no symptoms of myasthenia gravis and since the left border of the mediastinum was not displaced laterally, the possibility of a thymic tumor seems too remote to merit discussion.

A tumor within the wall or lumen of the esophagus of such a size would certainly cause difficulty in swallowing and anterior displacement of the trachea, neither of which occurred.

Erosion and widening of ribs are among the classic signs of aneurysm, and this mediastinal mass has caused both. However, fluoroscopically visible pulsations within the mass and pain and

peripheral vascular abnormalities would be almost equally classic for an aneurysm in this location, but they are not recorded.

Cystic embryonic arrests, such as dermoid and bronchiogenic cysts, cannot by the fluid nature of their contents exert sufficient pressure to erode solid structures without themselves showing evidence of altered configuration. This mass showed no alteration of contour. A solid embryonic arrest, such as a teratoma, might cause pressure phenomena, but would usually be irregular in outline or exhibit some localized area of calcification. Most embryonic arrests are found in the anterior mediastinum, and that is contrary to the evidence in this case.

Tumors of neurogenic origin are not uncommon in the mediastinum. One type, von Recklinghausen's disease, may occur as a local example of a generalized disease. When so found, it represents an extension from the neural canal, and is accompanied by erosion of the vertebral articular facets. The diagnosis is untenable here because the facets were not eroded and there were no other stigmas of the disease.

A second type of neurogenic tumor characteristically arises asymptomatically in the posterior mediastinum as a round dense mass, and by growth and pressure produces widening and erosion of the ribs in the costovertebral gutter. By reference to the record it is seen that a description of the typical features of this type of tumor is essentially a summary of the case under discussion. I shall therefore state my diagnosis as neurofibroma of the mediastinum.

Dr. Robbins: I entirely agree with Dr. Adams's diagnosis but I think it is only fair to tell him something that is not given in the abstract, or for that matter in the original record. The resident who did the fluoroscopy thought that this mass changed in size with change in position. This was scoffed at because it did not show in the films.

Dr. Adams: If it is true that the mass changed in configuration with change in position this indicates that it was not a solid lesion but a cystic one. That is a valuable bit of evidence. It would also indicate that the fluid was under enough pressure to erode solid structures. That is most unusual for a benign cyst such as a dermoid. I do not believe it could occur in a cyst of bronchiogenic or tracheal origin without displacement of the soft-tissue structures. A teratoma that started in a relatively benign fashion and then assumed malignant potentialities might have existed for a considerable time in the posterior mediastinum causing erosion in the way described and then might have grown rapidly with fluid in it.

Clinical Diagnosis

Neurofibroma of mediastinum.

Dr. Adams's Diagnosis

Neurofibroma of mediastinum.

Anatomical Diagnosis

Cyst of mediastinum.

Pathological Discussion

Dr. Tracy B. Mallory: The preoperative diagnosis on the wards was neurofibroma. I will read a portion of Dr. Robert K. Brown's operative note.

> Approximately 25 cm. of the fifth rib was resected subperiosteally and the pleura opened. The lung was not adherent. In the upper portion of the right thorax lay an ovoid, pink, thin-walled cyst measuring 7 by 8 by 12 cm. No solid content could be felt in it. About half the cyst was retropleural, lying against the superior mediastinum, with the lower border in the angle between the azygos vein and the superior vena cava. The cyst was removed by sharp dissection, several small vessels being tied in the process. It lay adherent to the superior vena cava as noted.

The cyst itself was, as the operative note indicates, very thin walled and partially translucent. The wall consisted of fibrous tissue with a lining of low cuboidal undifferentiated epithelial or possibly mesothelial cells. It lay external to the pleura but in contact with it, so it could have been a pleural cyst, although its actual position was in the mediastinum. Certainly it was not a dermoid or tracheal cyst. It had no connection with the trachea or bronchi.

Dr. Adams: How does the X-ray Department explain the findings?

Dr. Robbins: It is the only case we have had of cyst of the mediastinum that showed rib changes.

Dr. Adams: One would not have the right, on the evidence, to make a diagnosis of simple cyst.

Dr. Robbins: No.

Dr. Adams: Or, I believe, any diagnosis other than neurofibroma, on the basis of experience.

Dr. Robbins: The one thing that was important was the observation of the resident, which was never followed up.

Dr. Benjamin Castleman: Could the rib changes have been due to anything else?

Dr. Robbins: As I look at the film, it seems as if the whole rib is abnormal, but there is also something that suggests erosion of the rib above, however. It may be congenitally abnormal.

Dr. William B. Breed: You do not know the source of the cyst?

DR. MALLORY: I cannot say with certainty. We called it a mediastinal cyst — a simple cyst. That does not mean much.

CASE 29162

PRESENTATION OF CASE

A twenty-four-year-old single engineer entered the hospital because of general malaise, fever and headache.

Approximately three weeks prior to admission, while at work, the patient felt weak and dizzy and had to return home. Several hours later he suffered with general malaise, a slight heavy "headachy feeling" and a temperature elevation to 99.6°F. During the next four days he rested, usually in bed, but felt well enough to take a physical examination for the army. During this period he suffered from nasal catarrh, occasional headaches and "fullness in the ears." Two and a half weeks before admission he suddenly felt worse; the nasal catarrh and postnasal drip became worse and his temperature rose to 103.5°F. He had no cough, chest pain, muscle or joint pains or urinary symptoms. His physician found the white-cell count to be 8000, with 80 per cent polymorphonuclear neutrophils, made a diagnosis of "grippe" and treated him with sulfathiazole by mouth. Several days later the patient entered a community hospital, where he ran a spiking temperature that frequently reached 103°F. and then was usually associated with shaking chills. The white-cell count averaged 20,000, with 90 per cent polymorphonuclear neutrophils, and blood cultures were positive for a nonhemolytic *Staphylococcus aureus*. The patient was treated with an intravenous course of sulfadiazine without success, and a focus of infection was never demonstrated. Chest x-ray films were said to have shown bronchitis and mastoid plates were negative. Agglutination tests for typhus, typhoid and paratyphoid fevers were negative. A lumbar puncture done four days prior to admission to this hospital showed an initial pressure of 170 mm. of water; the dynamics, protein and sugar levels and cell count were not reported.

The family history was noncontributory. As a boy, an eardrum was lanced for otitis media without known sequelae. Recently the patient had been subject to frequent grippy colds. There was no history of rheumatic fever.

Physical examination disclosed a pale, thin, sick man who moved about slowly. The neck seemed stiff on forward flexion, but movements were not painful. Both eardrums were retracted, with slight reddening of the centers. The heart was slightly enlarged to the left, the apical impulse being felt in the fifth intercostal space, where a soft systolic murmur was audible. The second pulmonic sound was sharp and reduplicated. The lungs and abdomen were normal. Slight tenderness was present over the spine at the level of the eighth dorsal vertebra. The neurologic examination was not abnormal.

The blood pressure was 130 systolic, 80 diastolic. The temperature was 103°F., the pulse 110, and the respirations 30.

The hemoglobin was 12.2 gm., and the white-cell count 14,000. The urine was acid, had a specific gravity of 1.015 and showed a green sugar test (the patient had recently received a glucose-saline infusion); the sediment contained 1 white cell and an occasional epithelial cell per high-power field. The prothrombin time was 33 seconds (normal, 18 seconds). A blood Hinton test was negative. Blood cultures repeatedly contained a coagulase-positive, hemolytic *Staph. aureus*. The nonprotein nitrogen was 20 mg., and the protein 5.7 gm. per 100 cc., and the chloride was 96.0 milliequiv. per liter.

X-ray films of the sinuses showed no definite evidence of disease. Those of the spine showed slight haziness of the ninth vertebra, but a definite lesion was not demonstrated and the disk space appeared to be of normal width. A film of the chest revealed a hazy density in the left midlung field that appeared to be in the upper lobe. There was also haziness close to the septum at the base of the left lower lobe, and a small amount of fluid was present in the left pleural cavity. There was no shift of the mediastinum, and the right lung field was clear. The heart was not definitely abnormal although the left border was prominent. In the flat plate of the abdomen the kidney outlines appeared normal. There was an area of density overlying the right sacroiliac joint that might have been within the bone. No abnormal gas or soft-tissue shadows were visible.

A lumbar puncture revealed no initial pressure. When the head of the bed was raised the pressure rose to 110 mm. Good cardiac and respiratory oscillations were never obtained, but on straining for ten seconds, the pressure rapidly and steadily rose to 200 mm. but fell immediately to 110 mm. Compression of one jugular vein produced no rise, but bilateral compression occasionally produced a slow unsteady rise to 140 mm. After release there was a slow irregular fall to 110 mm. Then with the patient in a semisitting position, 10 cc. of clear, colorless spinal fluid was obtained; this reduced the pressure from 110 to 65 mm. The fluid contained 8 red cells, 2 large round

cells and 1 small round cell per cubic millimeter, and the total protein was 26 mg. per 100 cc.

The patient was treated with large doses of intravenous and intramuscular penicillin and adequate courses of orally administered sulfathiazole and sulfadiazine. However, he continued to run a spiking fever, became more ill and had shaking chills. The dorsal vertebral tenderness seemed to clear. The white-cell count ranged to 24,600. Occasionally a + test for albumin developed in the urine, and at such times the sediment contained a few red and white cells. An x-ray film of the chest on the forty-eighth hospital day disclosed mottled density in the base of the right upper lobe and new areas of density in the left lung, and there appeared to be small areas of rarefaction in the areas of density previously described. There was fluid in both pleural spaces and when this was aspirated from the left side it was found to be slightly blood tinged, but negative on culture.

Throughout his entire illness the patient suffered with frequent shaking chills and areas of consolidation developed in various parts of the lung fields. Examinations of the heart revealed only the apical systolic murmur heard on admission, though later a gallop rhythm developed. Repeated electrocardiographic recordings were within normal limits. Terminally, abscesses developed in the left lung and the sputum contained *Staph. aureus*. Albuminuria developed, and the urinary sediment contained red and white cells and sulfadiazine crystals. Four days prior to death he was treated with 25 gm. of sodium sulfadiazine administered in a 500-cc. saline infusion; this produced a blood level of 101 mg. per 100 cc. On the next day the urine showed a +++ test for albumin, occasional red and white cells and many sulfadiazine crystals. The nonprotein nitrogen was 82 mg. per 100 cc., and the chloride 95 milliequiv. per liter.

Two days prior to death the patient became cyanotic, and later comatose. A tension pneumothorax on the right side was relieved by suction. Several hours before death, subcutaneous emphysema of the chest developed; dyspnea suddenly increased, and he rapidly failed, dying two months after admission.

Differential Diagnosis

Dr. William Beckman: The symptoms of malaise and fever, the spiking temperature and rapid pulse, and the high white-cell counts all indicate that this patient was suffering from sepsis. The numerous blood cultures that were positive for staphylococcus make it fairly evident that the sepsis was due to this bacterium. That is further confirmed by the fact that the strain was coagulase positive, such staphylococci being more frequently pathogenic than the coagulase-negative ones. Of course staphylococci do not just develop in the blood stream: one must search for some source from which they might have been entering it. This site is not obvious from any of the data presented in the case record. However, the onset with a cold and definite ear involvement suggests that it must have been something that arose in the ear. The obvious thing to think of with middle-ear infection is mastoid involvement, but we have a clear statement from the x-ray examination that the mastoid processes were not involved, so this seems improbable.

The next thing one would think of is thrombosis of a lateral sinus. This could occur with minimal ear disease, the infection being transmitted from the ear to the sinus through small veins, with the formation of a septic thrombosis. The fact that he had a stiff neck is suggestive of this. I think that is what the patient had. At least it is the best I can do in discovering the primary focus on the basis of such information as we are given in the case.

Incidentally, the lumbar-puncture findings are perfectly satisfactory for the diagnosis of sinus thrombosis. The fact that jugular compression did not produce a rise in pressure is suggestive, though not diagnostic. Certainly cases of sinus thrombosis have been reported in which there was no more cellular response in the spinal fluid than there was in this case.

If we postulate that the patient had a sinus thrombosis, and if it was infected with staphylococcus, it is easy to understand the staphylococcal septicemia, and all the other features of the case can be explained on that basis. We have definite x-ray evidence of increasing infection in the lungs, which probably means that emboli were being sent from the infected thrombus to the lungs from time to time, thus producing more and more abscesses. This is a good time to look at the x-ray films.

Dr. Laurence L. Robbins: Only the films that show the course of the lung changes as the disease progressed are presented. On the first examination there is comparatively little to be seen in the chest. There is a small amount of density in the left costophrenic angle, suggesting fluid there. There is this shadow in the left midlung field, which is consistent with infarct. There are also finely mottled areas suggesting atelectasis in the right lung field but nothing about which one can be positive. Then as the disease progressed we see that new areas of density appear, as well as a large area on the right side. About a month after he had been in here we were fairly sure that there were cavities in the areas of density and that the areas

represented septic infarcts. The terminal film shows that there is pneumothorax as well, but since it was taken with a portable machine, it is not too satisfactory.

DR. BECKMAN: Can you tell anything about the density of the ninth dorsal vertebra?

DR. ROBBINS: We were never sure that the density meant anything, and it never was followed further.

DR. BECKMAN: I do not see how it fits in with anything I know about this patient. Possibly I am missing an important clue.

In addition to the fact that we have this excellent roentgenological evidence of continuing metastatic infarction of the lungs, it appears to me there is similar evidence of metastatic disease of the kidney. We know there were organisms in the peripheral blood because they were grown in blood cultures, and logically one can surmise that they would go to the kidneys too. From time to time the patient showed small amounts of albumin in the urine associated with red and white cells, and I think it is proper to consider that these findings represent metastatic infection of the kidneys. In addition, however, he was receiving the sulfa drugs, which we know damage the kidney, and later on in the disease he showed drug crystals, which might have accounted for some of the red cells, white cells and albumin present at that time. When I first read that the patient was given 25 gm. of sodium sulfadiazine at one time, I thought it might be a misprint, but when I saw that he had a blood level of 101 mg. per 100 cc. I knew it would be impossible to have two such misprints in the same sentence; so I presume that that dose of sulfadiazine was administered. I know nothing about the indications for such enormous doses. I feel sure that here it was a heroic measure in a patient obviously dying. The reason we do not know more about this method of therapy is that few of us have the courage to try large doses. However, with such a high blood level and with many crystals in the urine it seems probable that some of the renal damage, particularly after this large dose, was due to sulfadiazine. The next day the serum nonprotein nitrogen had risen and there seems to have been a rapid change in the kidney situation at that time, which further suggests that the drug had injured the kidney.

Another organ that is apt to be involved in cases of septicemia is the heart. Usually it is involved in the form of acute endocarditis. So far as I know, there are no special signs or symptoms of acute endocarditis. There was very little change in the heart throughout the entire course of the illness that could not be accounted for by the fact that the patient was going downhill, and I do not see how one can rule in or out acute bacterial endocarditis due to staphylococcus. But I shall say that he did have it, since it is highly probable that a staphylococcal septicemia for two months would result in such a lesion.

The final episode seems to have been a rupture of one of the lung abscesses into the pleural space, producing a pneumothorax with some sort of valve mechanism because the pneumothorax was under tension and had to be relieved by tapping the chest. I should also guess he had empyema if an abscess had ruptured into the cavity. I do not believe, however, that coma is a symptom of spontaneous pneumothorax; that probably has to be explained in another way, most likely by a terminal meningeal involvement by the staphylococcus.

So to sum up I shall say that the patient had a middle-ear infection that led to thrombosis of the lateral sinus, which in turn gave rise to staphylococcal septicemia with metastatic abscesses in the lungs, acute endocarditis, metastatic infection of the kidneys, terminal rupture of an abscess of the lung into the pleural space with empyema and, finally, invasion of the meninges.

DR. PAUL D. WHITE: If the lung involvement was due to septic infarction, the emboli would not have gone through the heart and lungs to the kidneys unless there was a paradoxical embolism by way of an auricular septal defect.

DR. BECKMAN: We know that there were organisms in the other side of the circulation because blood cultures from the arm vein were positive.

DR. CHAMP LYONS: May I add a note to that? I have been a long time trying to convince myself that it is true. We have had a patient without left-sided endocarditis who had petechiae of the skin and who, at autopsy, showed kidney abscesses of the infarct type. He had septic pulmonary lesions with secondary pulmonary venous thrombosis, which served as a source of septic emboli.

DR. TRACY B. MALLORY: It is a possible, but on the other hand not usual, source of widespread miliary emboli.

DR. LYONS: It is rare, but I have seen it.

DR. WHITE: I saw this patient several times because of the obscurity of the site of infection. I never found any proof of heart disease, but thought that there might have been right-sided endocarditis. Since the pulmonary valve never caused murmurs and since one does not expect to get murmurs when the tricuspid valve is involved, I postulated a tricuspid lesion.

DR. LYONS: I believe we committed ourselves to a diagnosis of right-sided endocarditis. So

far as our experience goes, such a persistently positive blood culture under penicillin therapy probably means endocarditis, and without other obvious foci we came to the diagnosis of right-sided endocarditis. I might add that, like other patients with staphylococcal bacteremia, this patient ran a persistently elevated prothrombin time, which we were able to control only with repeated blood transfusions. The massive sulfonamide dosage was a desperate effort undertaken at the request of the man's father, who was a physician.

Clinical Diagnoses

Vegetative endocarditis of tricuspid valve.
Staphylococcal bacteremia.
Multiple septic pulmonary infarcts.
Pyopneumothorax, right.

Dr. Beckman's Diagnoses

Otitis media, purulent.
Sinus thrombosis.
Bacterial endocarditis, acute (staphylococcus).
Septic infarction of lungs, with abscess formation.
Abscesses of kidney.
Pyopneumothorax.

Anatomical Diagnoses

Endocarditis, tricuspid valve, acute (*Staphylococcus aureus*).
Infarcts of lungs, multiple, septic, with abscess formation.
Rupture of abscess, with pyopneumothorax.
Emphysema, subcutaneous, of chest wall.
Acute glomerulonephritis.
Sulfonamide crystals in urinary tract.

Pathological Discussion

Dr. Mallory: I am not able to prove whether Dr. Beckman's primary diagnosis is right or wrong. We were not permitted to examine the head. We did find, however, endocarditis of the tricuspid valve, with a vegetation measuring 1 by 2 by 3 cm., which was so big that it projected up into and partially filled the auricle. There were no vegetations on the other valves. The lungs showed multiple septic infarcts in all stages of development, and one of them had ruptured into the pleura, causing pyopneumothorax.

The kidneys, of course, were of interest. We were able to find practically no evidence of sulfadiazine damage except for the presence of crystals in the pelves; there was nothing in the parenchyma that one could attribute to the drug. On the other hand, every glomerulus was swollen and contained more nuclei than it should, and I think we have to make the diagnosis of acute glomerulonephritis. We are accustomed to associate glomerulonephritis with streptococcal infection and it is certainly a rare concomitant of staphylococcal infection. Every glomerulus showed diffuse involvement, not the focal embolic involvement that one sees with bacterial endocarditis of the left side of the heart.

Dr. White: How often do you find evidence of previous rheumatic involvement of the valves in these cases?

Dr. Mallory: I think that in most cases the valves have seemed normal except for the acute endocarditis. There was no suggestion here that the tricuspid valve had been previously damaged.

I rather hurriedly looked up a number of our cases of primary bacterial tricuspid endocarditis, which are not very numerous, and found that my impression that the pneumococcus was the most usual organism was apparently correct. Over half the cases were due to the pneumococcus; next to that came the staphylococcus, with the streptococcus running third.

Dr. Beckman: You do not know what the defect was in the dorsal vertebra?

Dr. Mallory: We could find nothing.

Dr. Lyons: It is only fair to add that we, on the wards, had the benefit of Dr. LeRoy A. Schall's opinion that sinus thrombosis could be ruled out with a fair degree of certainty.

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THE SOCIOECONOMIC BURDEN OF CRIPPLING DISEASES

The burden of the crippling diseases is growing heavier. The average duration of chronic diseases in persons over fifty years of age has more than doubled in twenty years. In 1870 seven persons were living in the productive years from twenty to sixty to one person in the nonproductive years after sixty. In 1930 there were only five and a half productives to one nonproductive, which represents a loss of 23 per cent in sixty years. As Bigelow and Lombard[1] stated, "There is hardly a family in Massachusetts without immediate experience with cancer, heart disease or rheumatism."

Excepting mental disease, the chronic and crippling diseases that are of chief concern to the sufferers themselves and to the taxpayers of any nation may be listed in the inverse order of their importance as follows: congenital defects and birth injuries, diseases of the locomotor and skeletal systems, tuberculosis, diabetes, nephritis and renal disorders, cancer, major cardiac and circulatory disorders, and chronic rheumatism. The findings of the careful and authoritative study of the incidence and the implications of chronic disease in Massachusetts were reported by Bigelow and Lombard[1] in 1933. They concluded: "Rheumatism . . . cripples in the largest number and kills in the smallest. This very ability to cripple without killing would seem to put it in the lead of all other chronic diseases as of pre-eminent social, economic and medical importance." Moreover they found that, with the exception of chronic diseases of the eyes and ears, the chronic rheumatic diseases were receiving the smallest amount of medical attention: over 68 per cent of persons affected by these diseases either were receiving no medical treatment or were treating themselves.

At the present time the facilities for early diagnosis, research, discriminating therapy, hospitalization, and undergraduate and postgraduate medical education are sadly inadequate to cope with this "king of human misery," who crippled the human prototype, the Ape Man, two hundred million years ago. But, as Bigelow and Lombard[1] stated: "The pall of hopelessness among the 'profession' in regard to effective therapy is even more atrophying than that of the public. . . . All resources, private, philanthropic and governmental, must be enlisted. Complacency is wicked and dangerous." These are strong words but they need more emphasis today than when they were written ten years ago.

An excellent editorial[2] on crippling diseases appeared in the January 30 issue of the *Lancet*. It defines crippling disease as a disorder that leads to incapacity, calling attention to the fact that the chronic rheumatic diseases probably lead to more

crippling, greater suffering and higher economic loss than do any other medical disorders. It has been estimated that more than a million patients in England annually consult physicians because of the chronic rheumatic diseases, which cause one sixth of the total invalidity of the insured population. The annual cost of these diseases in England and Wales is believed to be at least £20,000,000, and an equally serious state of affairs has been found to exist in Scotland. In 1935 it was estimated that in the United States, disability resulting from the chronic rheumatic diseases represented an annual wage loss of more than $200,000,000, and it was said that in 1931 about 35,000 ex-service men received over $10,000,000 in disability compensation for arthritis and that the figure was increasing yearly.[3]

The Empire Rheumatism Council, of which Lord Horder is chairman, the British Orthopaedic Association and the Scottish Orthopaedic Council have advocated the establishment of one or more special hospitals for the treatment of the crippling diseases in each medical region of Great Britain as a means of lightening the social and economic burden of these crippling diseases.

Several years ago Dr. Frederick A. Washburn, formerly director of the Massachusetts General Hospital and subsequently commissioner of the municipal hospitals of Boston, suggested as a result of his experience, and for what seem to be cogent reasons, that units for the investigation and treatment of the crippling diseases should be established and administered by a large general hospital of high standing that was affiliated with an important medical school. Under such a plan the cost of building and administration would be greatly reduced, diversified laboratories would provide opportunity for research, consultants in medicine, surgery and the specialties would be available daily, the training school would solve the nursing problem and undergraduate and postgraduate education would be made easy. The conviction is growing that Dr. Washburn's plan is sound. In such units the chances of finding the solutions of some of the vexing problems that the crippling diseases present would be much better than they would be in the special hospitals proposed by the *Lancet*. Today, solutions are paramount and should be the order of the day.

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AMERICAN MENTALITY RE-ESTABLISHED

As UNREPENTANT, even if untutored, practitioners of the basic art of psychology, we physicians of the family front should show a particular interest in the issue of *Fortune* for December, 1942. In this number our opulent contemporary goes all out on a crusade to end once and for all the unhappy determination of the majority members of the American public to classify the other adult millions as possessing the average intelligence of thirteen-year-old children. Such a belief, now branded by *Fortune* as an outrageous libel, dates back to World War I, when large groups of American troops scored an average mental age of thirteen years in the Binet intelligence test. Since that time the average American, although convinced that he himself knows his way around,—and how,—has pityingly accepted for his colleagues in the art of living the intellectual status that had been so enthusiastically established for them.

This myth has, of course, its value, for in each of us a decided sense of well-being results from the consciousness of our superiority to the impotent proletarian ground swell that continually breaks against the solid foundations of our ego; it is another matter when the press, the radio, Hollywood, the advertising fraternity and even our representative, if somewhat zealous, government adopt the same attitude.

That attitude on the part of all these agencies probably had its uses when the road was relatively smooth and each gas tank was full to overflowing. It showed, in fact, a smartness not usually attrib-

uted to the thirteen-year-old mentality — we were willing to let someone else do the worrying when there was little or nothing to worry about. Childish behavior, too, in moments of relaxation, which has been taken to indicate a goon-like vacuity, is by no means the high sign of a childish mentality. Our national sense of humor is a powerful defense that our grimmest enemies have never yet been able to penetrate.

When reality does present itself, however, we prefer to be allowed to face it as such. As a nation and as individuals we have come of thinking age and have a right to expect a mature approach. We have a right to be told our bad news without sugar-coating — good or bad, it belongs to us. We have a right, rarely granted, to listen to radio programs without being harried by hypophrenic advertising plugs. We have a right to expect that our leaders, elected, appointed or self-selected, will treat us as fellow citizens and not as particularly helpless babes in the wood; that they will be leaders and not drivers, executive officers and not police officers.

We have a right not to be talked down to as children, but to have our problems and our obligations explained in clear and simple terms, free of legalistic indirection. We have a right to be told, by acknowledged experts, the state of our natural resources and our individual relations to them; we have a right, after we have cheerfully accepted the rationing of any commodity, to be allowed the free use of it, within that restriction, without being forced to accept the outrage of being spied on, bullied and police-ridden — this, happily, is at last coming to pass. We have, moreover, the right to ask for a clear and sensible definition of that bedeviling term "pleasure driving" or that its use be dropped for the duration!

MEDICAL EPONYM

Trendelenburg Position

This was described by Friedrich Trendelenburg (1844–1925) of the University of Bonn in an article entitled "Ueber Blasenscheidenfisteloperationen und über Beckenhochlagerung bei Operationen in der Bauchhöhle [Operations for vesicovaginal fistula and elevation of the pelvis in abdominal operations]," which appeared in Volkmann's *Sammlung klinischer Vorträge* No. 355 pages 3373–3392, Leipzig, 1890.

> If the patient's body is so placed on the operating table that the symphysis pubis is the highest point of the trunk, and the axis of the trunk forms an angle of at least 45° with the horizontal, then all the viscera, but especially the liver, spleen and mesentery, fall by their own weight into the hollow of the diaphragm. The intestine follows and falls out of the true pelvis, so far as air pressure permits. . . . If one now makes either a longitudinal or horizontal incision in the hypogastric region for the purpose of removing a stone, and splits the recti together with the underlying fascia, air will immediately enter into the prevesical space, often with an audible sound. The peritoneal fold drops down, and the narrow prevesical space becomes a gaping, well-lighted cavity in which the anterior wall of the bladder and the surrounding fold of peritoneum may be seen. . . . The value of elevation of the pelvis is equally striking in intraperitoneal operations in the pelvic cavity and the lower part of the abdomen. . . .

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

Intestinal Obstruction in a Newborn Infant

S. M. was the first child of a normal mother and father. Pregnancy had been uneventful and delivery occurred at full term after a short and easy labor. The birth weight was 5 pounds, 12 ounces. Twenty-four hours after delivery, when the child was put to the breast, she nursed normally but vomited shortly afterward. The vomitus contained mucus and milk curds. Slight cyanosis was noted, and although physical examination was normal, a roentgenogram of the chest showed partial atelectasis of the left upper lobe. The vomiting was considered of no significance, but the atelectasis caused some concern. However, on the second day of life the child's color improved and a check roentgenogram showed the lungs to be well expanded. During the second and third days of life vomiting continued and became definitely projectile in nature. Apparently the vomitus did not contain bile. Gastric lavage had no beneficial effect. On the second and again on the third day a meconium stool was passed.

Physical examination at the age of three days showed an infant who was normal in appearance

except for slight dehydration. There was no generalized distention of the abdomen — in fact, the lower two thirds of the abdomen was quite flat. The epigastrium was somewhat full. Close inspection showed a few visible peristaltic waves, apparently gastric in type, passing from the left to the right side of the epigastrium. No abnormal masses could be felt within the abdomen. By auscultation the lungs appeared to be well aerated.

The red-cell count was 5,000,000, with a hemoglobin of 100 per cent, and the white-cell count 7600. Roentgenograms of the abdomen were taken with the child in a prone and also in an erect position. These showed considerable gaseous dilatation of the stomach, in addition to a large bubble of air that presumably represented a dilated first part of the duodenum. No gas could be seen in the abdomen below this level. The findings were suggestive of a duodenal obstruction, and it was deemed advisable to explore the child without further study by a gastrointestinal barium series.

Operation was undertaken under local novocain infiltration of the abdominal wall. The stomach was dilated, and the pylorus patulous. The first portion of the duodenum was enlarged to about three times its normal diameter. The pancreas extended far to the right, and its head surrounded the second portion of the duodenum — a so-called "annular pancreas." This constricted and obstructed the duodenum. Only a few small bubbles of gas were present in the tiny, collapsed intestine beyond the second part of the duodenum. The lumen of the duodenum at the point of obstruction was not more than a millimeter or two in diameter. So far as could be seen, the extrahepatic biliary system was normal. To relieve the duodenal obstruction, an antecolic, isoperistaltic duodenojejunostomy was performed, using two layers of fine silk to effect the anastomosis. The baby stood the procedure well and was returned to bed in a satisfactory condition.

For the first two postoperative days all fluids and nourishment were given by parenteral routes. On the third day she was placed on two-hour feedings, beginning with water, changing to whey, and finally employing breast milk. After the fourth day a cow's milk, Karo and water formula was used, increasing the volume of the feedings and increasing the time interval between feedings, so that the baby was taking full caloric requirements on a four-hour schedule at the time of her discharge from the hospital on the eighth postoperative day. The abdominal wound healed per primam.

Following discharge the baby has taken feedings normally, has had a satisfactory gain in weight and has progressed normally in every way during the six months that have elapsed since operation.

Comment. Intestinal obstruction in the newborn infant may be due to a variety of causes. In this case an unusual one was encountered, but whether the obstruction is due to such a rare anomaly or to some other cause, such as malrotation of the bowel, mesenteric band, congenital stenosis or atresia, imperforate anus or meconium ileus, the manifestations tend to be more or less similar, depending on the degree of obstruction and the level at which it occurs.

Because most of these conditions are amenable to skillful surgery an early diagnosis is of primary importance. This begins with a knowledge of the etiologic possibilities that may underlie what at first appear to be minor symptoms. With a suspicion of this sort, the physician should question the nurses regarding the mechanical aspects of feeding and then carefully observe the appearance of the abdomen. Because the neonatal intestine normally contains so much air, helpful assistance can be gained from a roentgenogram. The anatomic level of obstruction can be substantiated by films taken with the infant in various positions; if the air-filled portion of the bowel terminates sharply at the same level when the infant is photographed suspended head downward as when a film is made in the normal upright position, the probability and the site of an obstruction become more definitely established. Meconium may be passed quite normally in the presence of high obstructions such as this one, so that although its failure to appear is significant, its presence does not alter the diagnostic probabilities.

The refinements of pediatric surgery now offer a considerable chance of successful result in operations on newborn and even premature infants. Unsuccessful results may be traced to delays in diagnosis as often as to any other single cause.

WAR ACTIVITIES

INDUSTRIAL MEDICINE

Tuberculosis in Industry

Seventy-seven war industries in 11 states were surveyed by the eight 35-mm. photofluorographic units operating in industry prior to February 1, 1943, reports the Office of Tuberculosis Control, United States Public Health Service.

A total of 194,896 individuals were x-rayed. Tabulations on results are available for 125,190 people. Of these 1631, or 1.3 per cent, were found to have significant pulmonary tuberculosis. The distribution of the positive cases by stages of the disease was as follows: 874, or 53.6 per cent, minimal; 707, or 43.3 per cent, moderately advanced; and 50, or 3.1 per cent, far advanced.

In the District of Columbia 28,098 government workers have been x-rayed. Exactly 300 cases of pulmonary tuberculosis have been discovered, an incidence of 1.1 per cent. Of these 182 (60.7 per cent) were minimal, 106 (35.3 per cent) moderately advanced, and 12 (4.0 per cent) far advanced. In addition, 1300 workers at the National Institute of Health have been x-rayed. Among these, 15 cases of tuberculosis were found — 9 minimal and 6 moderately advanced. — Reprinted from *Industrial Hygiene* (March, 1943), a bulletin issued monthly by the division of Industrial Hygiene, United States Public Health Service.

MISCELLANY

WAR CHALLENGES THE GENERAL PRACTITIONER

Fire is fire, no matter what the fuel, but when gasoline is thrown on a flame a dangerous explosion results. Tuberculosis is the same disease now as in peacetime, but war invariably favors a flare-up of tuberculosis and creates new difficulties for those who must combat the blaze. The hard-pressed general practitioner is a seasoned fire-fighter whose aid must be enlisted and whose effort must be supported if smoldering tuberculosis, lately coming under control, is to be prevented from spreading into a serious conflagration. Even veteran firemen, however, periodically examine their equipment and drill themselves to increase their efficiency. A recent article (Geary, P. General Practitioner's Role. *Bulletin of the National Tuberculosis Association*, March, 1943) emphasizes many of the important points and is abstracted below.

Under the stress of war it has been observed that conditions favor the spread of pulmonary tuberculosis. Probably an increase in the disease has not occurred to date in this country as a whole, but a rise has occurred among other belligerent nations and in some of our own industrial centers.

Increase in prevalence and mortality can be traced to inadequate diet, insufficient institutional facilities and medical care, lowering of resistance from apprehension and disturbed rest, and overcrowding and poor housing in areas of concentrated war industry.

Since the disease appears on the increase in countries at war for some time, it must be assumed a similar trend is to be anticipated here. This calls for early diagnosis, hospitalization of active cases and discovery of infective contacts. Greatest hope for success lies in the interest and co-operation of the general practitioner. He sees the patient early and through his intelligent effort will come early diagnosis, prompt isolation and the investigation of contacts. Toward this goal a path is indicated for the practitioner, who, deprived of many a colleague, finds his problems multiplied and his strength and time in no wise reinforced.

Usually it is easy for a tuberculous specialist to make a diagnosis once the suspect has been singled out by the practitioner. More difficult is it for the latter to give due consideration to tuberculosis — only one of many conditions that may assail his patient.

For example, cough is the commonest symptom of the disease. In one with a history of previous acute pleurisy, chronic cough is suspicious. Nevertheless, the disease may be present without it, and most agree that cough or any other symptom is a relatively later, not an encouragingly earlier, manifestation of pulmonary tuberculosis. If one persists in describing tuberculosis in terms of symptoms, one might as well omit further discussion of *early* diagnosis, even though it is admitted that knowledge of classic symptoms is essential if one is to have tuberculosis in mind when encountering those less fortunate cases long past the stage when early discovery was possible. These symptoms include fatigue, particularly in the late afternoon, loss of weight, low-grade fever, chest pain and hemoptysis.

If tuberculosis is to be found preclinically or at onset of its earliest symptoms a thorough, practical and economical plan of attack is necessary. Weapons at hand include history, physical examination, tuberculin test, sputum examination, x-ray films and fluoroscopy.

Tuberculosis specialists generally believe that the greatest deterrent to early diagnosis by the practitioner is the expense of x-ray examination. If it were as easy to x-ray the lungs as to do a physical examination many more early cases would be found. Where x-ray facilities are handy it is simpler to take a picture and study it than to do a physical examination, which, though thorough, may fail to disclose the trouble. Most practitioners lack office x-ray facilities, but the truth remains there is no substitute for a good x-ray picture. Today, in all but the most rural communities, arrangements can be made for x-ray films of the chest in the indigent as well as in others.

Physical examination may uncover rales, breath sound changes and so forth, but their absence does not mean absence of tuberculosis. In every sanatorium are patients with far-advanced disease who have been told by their family doctors that no signs of tuberculosis were present. Similar oversight may occur in some early cases when symptoms are present as well as positive x-ray findings. This is no reflection on the skill of the physician but proves that symptoms and x-ray evidence are often present before definite physical signs of tuberculosis develop.

Fluoroscopy, even in the hands of experts, is not so accurate as film methods in diagnosing tuberculosis. Serial pictures, too, give better clues concerning the progress of lesions than does mere observation of the clinical record.

The tuberculin test, variously conducted, is of value in the process of screening groups or studying individuals. A positive test shows that the skin has been sensitized by previous or present tuberculous infection. It does not prove that active pulmonary disease is present, but does call for an immediate x-ray film of the chest. A negative test, conversely, is almost conclusive that active tuberculosis does not exist. There are exceptions to this statement, but they are rare.

Sputum examination is vital. A positive sputum leaves no doubt that active disease is present, but a negative sputum is no guarantee of its absence. There may be relatively few bacilli in a sputum sample; improper collection may provide saliva instead of thick material truly expelled from the lung by a spell of coughing; or too few samples may be examined. Reinforcing the simple smear are concentration methods, culture or guinea-pig inoculations, and examination of the fasting gastric sediment in those swallowing their sputum.

Tuberculosis cases should be reported promptly to the public-health authorities who assist in determining their disposition.

Many practitioners are not interested in treating tuberculous patients. Others feel they see cases so rarely that they would welcome assistance by experts. Sanatorium care,

if available, promises conditions ideal for treatment and training of the patient and protection of his family and friends.

People who contract pulmonary tuberculosis usually do so because of intimate exposure to someone with a positive sputum. Thorough search is made in the patient's household and among his other associates, each being tuberculin tested and the positive reactors x-rayed. Obviously the x-ray film, if showing nothing at first, should be repeated at four-month intervals for several years, as breakdown may be slow to appear.

Many countries have well-organized tuberculosis associations whose nurses serve as fieldworkers. Granted this aid, the social side of the problem can be handled with personal home interviews and transportation of the patient and of the contacts to the sanatorium or clinic for testing and x-ray. Tuberculosis workers are well trained and function to give the practitioner able service and advice about the disposition of the case, in the adjustment of the family and in the follow-up of the patient once he leaves the sanatorium.

The family doctor should co-operate with those who have directed the treatment when he receives back the discharged case. Rehabilitation in these people is complex and important. Many sanatoriums have personnel specially trained to instruct patients in occupations they will be fitted to carry on after their cure, or to prepare them for the special problems facing them on their return to society. The family doctor must continue his interest through both treatment and rehabilitation periods, with periodic check-up, assurance and advice.

The greatest contribution the general practitioner can make in the field of tuberculosis in wartime is the intensification of his peacetime effort, keeping the disease constantly in mind and remembering that the ultimate ideal in controlling tuberculosis would be to have every adult x-rayed annually. — Reprinted from *Tuberculosis Abstracts*, April, 1943.

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR FEBRUARY, 1943

Diseases	February 1943	February 1942	Seven-Year Median
Anterior poliomyelitis	0	2	0
Chicken pox	1280	1651	1438
Diphtheria	9	11	12
Dog bite	520	474	531
Dysentery, bacillary	6	3	6
German measles	3490	261	80
Gonorrhea	345	326	326
Measles	2661	1753	1896
Meningitis, meningococcal	52	12	8
Meningitis, other forms	7	14	*
Mumps	1113	1930	777
Paratyphoid infections	3	4	2
Pneumonia, lobar	323	477	579
Scarlet fever	2081	1399	1002
Syphilis	363	374	405
Tuberculosis, pulmonary	177	223	179
Tuberculosis, other forms	16	14	21
Typhoid fever	3	6	5
Undulant fever	1	5	4
Whooping cough	658	779	779

*Pfeiffer-bacillus meningitis only other form reportable previous to 1941.

Geographical Distribution of Certain Diseases

February, 1943

Diphtheria was reported from: Boston, 2; Chelmsford, 1; Fall River, 4; Foxboro, 1; Lowell, 1; total, 9.

Dysentery, bacillary, was reported from: Boston, 6; total, 6.

Encephalitis, infectious, was reported from: Pittsfield, 1; Somerville, 1; total, 2.

Lymphocytic choriomeningitis was reported from: Fort Banks, Winthrop, 1; total, 1.

Meningitis, meningococcal, was reported from: Adams, 1; Belmont, 1; Boston, 3; Brockton, 1; Cambridge, 1; Camp Edwards, 8; Chelsea, 1; Chicopee, 1; Everett, 1; Fall River, 1; Falmouth, 2; Fort Banks, 1; Fort Devens, 2; Hanson, 1; Holyoke, 1; Leominster, 1; Medford, 1; Newton, 2; Rehoboth, 1; Revere, 1; Salisbury, 1; Shrewsbury, 1; Somerville, 2; Spencer, 1; Stoneham, 1; Taunton, 1; Waltham, 1; Wareham, 2; Webster, 1; Westover Field, 2; Weymouth, 1; Winthrop, 1; Worcester, 5; total, 52.

Meningitis, other forms, was reported from: Beverly, 1; Boston, 1; Newton, 1; Northbridge, 1; Woburn, 1; Worcester, 2; total, 7.

Paratyphoid fever was reported from: Salem, 1; Wakefield, 1; Westminster, 1; total, 3.

Septic sore throat was reported from: Amesbury, 1; Attleboro, 2; Boston, 1; Cambridge, 2; Newton, 1; Salisbury, 1; Swampscott, 1; Wakefield, 1; Winchester, 1; Worcester, 1; total, 12.

Trachoma was reported from: Boston, 1; total, 1.

Trichinosis was reported from: Boston, 1; total, 1.

Typhoid fever was reported from: Stoughton, 2; Wellesley, 1; total, 3.

Undulant fever was reported from: Southwick, 1; total, 1.

The trend upward of certain diseases, noticeable for several months past, continued during February. Meningococcal meningitis reached a record high for the month of February. Scarlet fever surpassed any February record, since 1906, with the exception of that of 1927. German measles set up a new high February record.

Above the seven-year median figure were German measles, gonorrhea, measles, meningococcal meningitis, mumps, paratyphoid fever and scarlet fever.

Under the seven-year median were diphtheria (next to the lowest February record), lobar pneumonia (with a new low record for February), chicken pox, dog bite, syphilis, tuberculosis (both pulmonary and other forms), typhoid fever, undulant fever and whooping cough. There were no cases of anterior poliomyelitis reported during the month.

DR. PRATT DECORATED FOR VALOR

Lieutenant-Commander Theodore C. Pratt (MC), U.S.N.R., a member of the surgical staff of the Massachusetts General Hospital and of the Palmer Memorial Hospital (on leave of absence), has been awarded the Navy Cross "for extraordinary heroism and distinguished service in line with his profession as chief surgeon of a division field hospital on Guadalcanal." The citation states that Dr. Pratt courageously operated on and supervised treatment of casualties while the hospital was being bombed by enemy planes and shelled by surface craft during last August and September.

(Notices on page x)